

Bioactive phytochemicals of jasmine oil and their role in managing hypertension: A combined clinical and *in-silico* study

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Abstract: Background: Jasmine oil massage has a thousand years of traditional history of curing and treating various ailments like hypertension, diabetes and muscle cramps without any sound pharmacological evidence. Traffic wardens have to stand throughout their duty hours, which can lead to muscle fatigue and compression and those suffering from stage 2 hypertension have to face worsened cardiovascular issues. **Objectives:** To assess the therapeutic effectiveness of jasmine oil massage, administered manually and in combination with an electrical massager, on blood pressure and related cardiovascular parameters in traffic wardens with stage 2 hypertension and to investigate the potential molecular interactions of key jasmine oil phytoconstituents with human voltage-gated sodium channels. **Methods:** The randomized controlled trial study (IRCT20230103057033N2) was conducted from November 2022 to March 2023. A total of 300 patients were randomly divided into three groups. Group A was treated with jasmine oil and an electrical massager. Group B was treated with jasmine oil manually. Group C was treated with only an electrical massager. The treatment regimen was 3 weeks, distributed as 6 sessions/week, each session lasted for 40 minutes. Blood pressure, blood cholesterol, respiration rate, heart rate and oxygen saturation of all the patients with hypertension were measured before and after treatment. The major phytoconstituents, phytosterol, α -pinene, benzyl acetate and linalool were docked with human voltage-gated sodium channels (Na^v1.9, Na^v1.8 and Na^v1.7). **Results:** Jasmine oil showed more significant results ($p = 0.0001$) in patients treated with jasmine oil and an electrical massager, significant results ($p < 0.005$) in patients treated with jasmine oil and non-significant results in patients treated with an electrical massager only ($p > 0.005$). Na^v1.9 exhibited slightly better binding across most ligands compared to Na^v1.7 and Na^v1.8, suggesting that this isoform may offer a more favorable binding pocket for phytochemicals were tested. **Conclusion:** The results support better drug absorption and effects when jasmine oil was applied with an electrical massager and project a newer, non-invasive alternative, less expensive and safer treatment protocol for traffic wardens suffering from stage 2 hypertension.

Keywords: Cholesterol; Cardiometabolic; Cardiorespiratory; Hypertension; Jasmine; Traffic wardens

Submitted on 26-07-2025 – Revised on 02-11-2025 – Accepted on 01-12-2025

INTRODUCTION

Hypertension is defined as high systolic blood pressure (SBP) with a value ≥ 130 mmHg and low diastolic blood pressure (DBP) with a value ≤ 80 mmHg. A person is considered hypertensive if their systolic blood pressure increases above 140 mmHg and their diastolic blood pressure increases above 90 mmHg (Humphrey *et al.*, 2021). According to World Health Organization (WHO) estimates, 1.28 billion people between 30 and 79 have hypertension and only one in five can control it (Kim, 2023). In the United States of America (USA), 90% of hypertension cases are primary. Secondary hypertension results from the associated ailment (Adonye *et al.*, 2024). Hypertension impairs renal natriuresis, the feedback system that lowers blood pressure by increasing kidney salt and water excretion. Poor renal function, incorrect

activation of hormones that control kidney salt and water excretion, such as the renin-angiotensin-aldosterone system (RAAS), or insufficient sympathetic nervous system activity can produce pressure natriuresis (Ma *et al.*, 2022). Persistent hypertension can cause cardiovascular disease and stroke, the world's leading killers (Perwasha *et al.*, 2022). Age, gender, social level, education, smoking, body mass index (BMI), ethnicity and access to primary healthcare all contribute to hypertension (Ma *et al.*, 2022). Family history, obesity and diabetes raise hypertension risk. Stress, increased sodium consumption and smoking can also cause hypertension. Patient education is paramount to effective management and must always involve specific instructions related to weight control, salt restriction, smoking management, adequate management of obstructive sleep apnea and exercise. Pharmacological

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therapy includes angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), diuretics (typically thiazides), calcium channel blockers (CCBs) and beta-blockers (BBs), which are given with consideration for age, race and comorbidities such as renal dysfunction, left ventricular dysfunction, heart failure and cerebrovascular disease (Jahan *et al.*, 2024). Cholesterol is a form of fat present in the bloodstream. The liver produces cholesterol for the body. Cholesterol can also be obtained from foods that a person consumes. Cholesterol is stored in the adipose tissue of our body and circulates in the bloodstream bound to proteins (Harrison, 2021). It can cause arteries to narrow, stiffen, or get blocked. If the blockage worsens over time, it can lead to a heart attack or stroke in adults. Low-density lipoprotein (LDL), known as "bad cholesterol," transports cholesterol from the liver into circulation, where it can attach to blood vessels. High-density lipoprotein (HDL), known as "good cholesterol," transports cholesterol from the bloodstream to the liver for breakdown (Yagoub *et al.*, 2022). Several lipid/lipoprotein irregularities have been associated with obesity and cardiac issues, collectively referred to as dyslipidemia; however, these dyslipidemias are frequently hyperlipidemias, in which the majority of lipids are pushed toward the upper limits of the range or beyond it (Griendling *et al.*, 2021). Dyslipidemia is a substantial risk factor for cardiovascular disease in people with raised total cholesterol (TC), triglycerides (TG), LDL and reduced HDL (Camargo *et al.*, 2021).

Jasminum sambac (L.) is a famous folkloric medicine of the Oleaceae family. It is widely used as an antioxidant, antimicrobial, anti-diabetic, anti-inflammatory, analgesic, antipyretic and cardiogenic (Khan *et al.*, 2021; Ain *et al.*, 2024). Jasmine oil is frequently used for massage and body shaping. Phytochemical studies of *J. sambac* showed the presence of essential oils, proteins, flavonoids, carbohydrates, resins, terpenes, glycosides, salicylic acid and many other valuable compounds (Ma *et al.*, 2022). Applying pressure to specific reflex points on the feet, which are thought to correspond to various organs and systems in the body, is the therapeutic technique of reflexology (Elmowafy and Gaber, 2024). The goal is to stimulate these reflex areas to support balance and general wellness. Rotation, pressure point massage and thumb and finger walking are some of the techniques. Cleaning and relaxing the feet come first in most sessions, then tension-relieving areas are identified and treated and the session concludes with a general foot massage (Anwar *et al.*, 2022). This electric foot massager provides a deep kneading Shiatsu technique that improves circulation and blood flow, thereby enhancing muscle recovery and reducing inflammation (Robinson *et al.*, 2011). Equipped with a rotation ball, rolling stick, heat therapy and air compression for ultimate relaxation and recovery. Fifteen minutes of massage is recommended to relieve plantar fasciitis, neuropathy, diabetic neuropathy,

chronic pain, hypertension, poor circulation and so much more (Atchison *et al.*, 2021).

As part of their daily operations, traffic wardens spend many hours standing, which puts stress on their musculoskeletal system and can lead to systemic issues (Afta *et al.*, 2023). This not only stretches the knees, but also strains long hours of standing, as it is associated with conditions of poor circulation leading to venous pooling, swelling and eventual fatigue in the legs. Such factors contribute to chronic pain and an increased predisposition to developing other conditions, including varicose veins (Ali *et al.*, 2021). Stage 2 hypertension, which is diagnosed with a blood pressure reading of 140/90 mmHg or higher, is severe and potentially life-threatening. Traffic wardens, for example, are among those most affected because their working environment exposes them to multiple risk factors that directly contribute to the development and progression of hypertension: Constant management of vehicular traffic, mediation between road users and work in an unpredictable and tense environment elevate stress hormones, such as cortisol and adrenaline (Skolarus *et al.*, 2023). Long-term exposure results in constant high blood pressure, leading workers to hypertensive states. Traffic wardens are kept on duty for long periods, often more than 8-10 hours a day, with limited rest. A sustained cardiovascular strain occurs during prolonged physical activity, such as standing and walking, under heightened alertness conditions. Such a stressful regimen greatly increases the risk for hypertension to arise or worsen over time. Repeated environmental exposures to toxic substances, thermal extremes and noise pollution generate further systemic stresses that directly contribute to cardiovascular risk (Tang *et al.*, 2022). The individual also tends to have irregular meal times and poor dietary choices, which often worsen when proper facilities are not available during shifts. Furthermore, dehydration is also a possibility due to scarcity of water availability and unscheduled breaks and this may again lead to circulatory system pressure (Permana and Lindayani, 2021).

In contrast, despite their high-risk profile, traffic wardens are often denied routine health screenings and interventions. Lack of education on hypertension management or the existence of services providing preventive care or policies monitoring workplace health even worsens the problem because, without timely treatment and change in lifestyles, the risk of developing complications such as heart attacks, strokes, or kidney damage becomes increasingly significant (Chen *et al.*, 2021). Dealing with non-compliance from motorists, roadside emergencies and generally working with the public can be a psychological strain that increases anxiety levels in traffic wardens. As one of the known risk factors for hypertension, chronic anxiety serves to further fuel the progression from borderline blood pressure readings to

advanced stages of hypertension, which includes stage 2 (Chen *et al.*, 2021). External stressors include environmental factors such as excessive heat, cold and air pollution, to which traffic wardens are exposed. These environmental conditions contribute to physical exhaustion and may also exacerbate inflammatory processes, thereby worsening osteoarthritis (OA) symptoms. Psychosocial stressors, including managing heavy traffic, resolving disputes and adhering to strict schedules, add an extra layer of mental fatigue that may indirectly exacerbate musculoskeletal conditions through the modulation of pain perception and stress responses (Chen *et al.*, 2021).

Furthermore, long work hours and unpredictable schedules limit a traffic warden's ability to maintain healthy lifestyle practices; these include regular exercise, wholesome dieting and rest. Access to health interventions, such as routine blood pressure monitoring and timely medical consultations, may also be limited due to demanding schedules or a lack of workplace health support systems. This lack of preventive care increases the likelihood of uncontrolled hypertension and associated complications (Atchison *et al.*, 2021; Chen *et al.*, 2021).

The main objective of this research is to assess the impact of deep-tissue foot massage on traffic wardens with stage 2 hypertension. Two different interventions have been used: one is manual massage supplemented with jasmine oil and the other is massage administered through an electrical massager. More specifically, it aims to evaluate the individual efficacy of each treatment modality (in terms of using jasmine oil-enhanced massage and electrical massage) in terms of improving physiological outcomes (blood pressure regulation, stress reduction and others) in comparing the effectiveness of these two approaches so that whether the inclusion of jasmine oil together with manual massage provides additional therapeutic benefits against a mechanical massage technique can be evaluated. By investigating the individual and combined effects of these interventions, this study aims to contribute to the evidence-based development of optimal stress and hypertension management approaches for traffic wardens and, hence, to occupational health solutions.

MATERIALS AND METHODS

Study design and settings

A lottery method, community-based, parallel-group, double-blinded, randomized control trial (IRCT20230103057033N2) was conducted. A prospective study was conducted from November 2022 to March 2023. The Helsinki Declaration was followed for research involving humans (Williams, 2008). Patient education was promoted through structured sessions that provided participants with thorough information about

their ailment, the purpose of the trial and the treatment procedures. Among the educational resources distributed to enhance understanding and encourage patients to actively participate in their treatment plans were visual aids. Participants also got the opportunity to ask questions and express concerns to ensure they were informed.

Sample size calculation

Sample size was calculated using OpenEPI statistical software (www.openepi.com). Two sided confidence level 95% and a 1% ratio of unexposed in sample while % chance of 80. % of unexposed without outcome 5.

Inclusion criteria

All patients signed a consent form for inclusion in the research. The inclusion criteria included the age group of 23–70 years (male and female), educated and uneducated, married and unmarried traffic wardens suffering from stage 2 hypertension.

Exclusion criteria

Persons with any type of mental or physical disability, lactating or pregnant females and any type of major surgery were excluded.

Equipments and materials

Mercury manometer (certeza), chol-check (best-check-9228), pulse oximeter (choice med digital), measuring tape, six ball head electrical massager (No7 palm control body massager electric body massager), jasmine oil (Mehmood Pharmaceuticals) were used in this study.

Randomization of participants

A total of 300 patients who were pre-diagnosed with stage-2 hypertension were randomly divided into three groups, A, B and C, by lottery method and a simple random sampling technique was used. Consolidated Standards of Reporting Trials (CONSORT) are presented in Fig. 1.

Molecular docking

Molecular docking simulations were performed to investigate the interaction between selected phytochemicals (α -pinene, benzyl acetate, linalool and phytosterols) and human voltage-gated sodium channels (Na_v1.7/SCN9A, Na_v1.8/SCN10A, Na_v1.9/SCN11A). Three-dimensional structures of the ligands were retrieved from PubChem in SDF format and converted to Protein Data Bank Charge Type (PDBQT) using Open Babel within the PyRx interface. The protein structures for Na_v1., Na_v1.8) and Na_v1.9 were prepared by removing water molecules and heteroatoms and by adding hydrogens and charges using AutoDock Tools. The docking grid was centered around the predicted active site or transmembrane region.

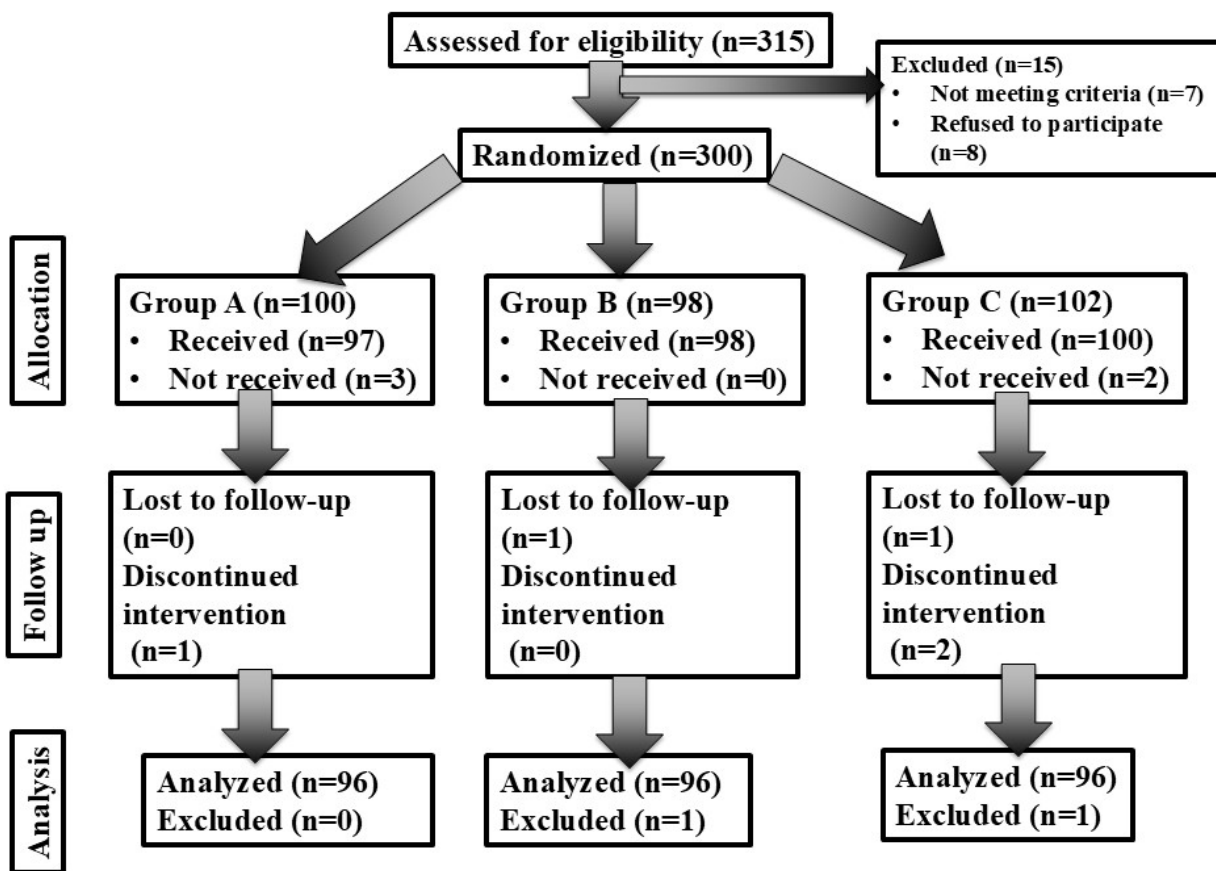


Fig. 1: CONSORT diagram showing the flow of participants through each stage of a randomized trial.

AutoDock Vina (embedded in PyRx) was used for docking and results were evaluated based on binding affinity (kcal/mol) and RMSD values.

Treatment protocols

A total of 300 patients were randomized into three groups. Group A (n = 100) was treated with an electric palm massage and a jasmine oil massage. Group B (n = 98) received a manual massage with jasmine oil. Group C (n = 102) was treated with an electric palm massager without jasmine oil. However, one patient from Group A discontinued intervention and one patient from Group B and group C failed to follow up (Fig. 1.) The total treatment duration was 3 weeks (6 sessions/week). Each session lasted for 40 minutes. We chose 6 sessions a week in the study to maintain an adequate dose of treatment that would cumulate while still making it consistent and feasible for the participants. The high frequency used in most massage therapy studies is in order to maximize intervention effect within a minimal time frame (Khan *et al.*, 2023). After three weeks, we compared pre- and post-hypertensive blood pressure and cholesterol levels. The CONSORT principles (Hopewell *et al.*, 2025) were followed by this study to guarantee thorough reporting and openness in the trial's planning, execution and analysis (Fig. 1). Heart rate, respiration rate, blood pressure and oxygen

saturation in pre- and post-treatment groups were measured. The conformation with the lowest binding energy and acceptable RMSD (preferably <2 Å) was selected for analysis (Khan *et al.*, 2024).

For Na^v1.7, four available PDB entries (5EK0, 6J8G, 6J8H and 6J8I) were comparatively evaluated. The 6J8G structure was selected for its superior crystallographic resolution (3.20 Å) and absence of unfavorable steric contacts with the docked ligands. For Na^v1.8, four structures (7WE4, 7WEL, 7WFR and 7WFW) were examined and 7WEL was chosen based on its high-resolution quality (3.20 Å) and well-defined transmembrane architecture. Since no experimentally resolved crystal structure is available for Na^v1.9, the AlphaFold-predicted model (AF-Q9UI33-F1) was utilized, which displayed a high-confidence pLDDT score (>90) across the major transmembrane regions. All protein structures were obtained from the RCSB Protein Data Bank (<https://www.rcsb.org>) and the AlphaFold Protein Structure Database (<https://alphafold.ebi.ac.uk/>). The selected models were screened to ensure structural integrity, biological relevance and absence of steric clashes or incomplete domains, ensuring suitability for subsequent docking analyses.

Protein preparation

Each protein structure was preprocessed to optimize it for molecular docking. Using BIOVIA Discovery Studio Visualizer 2021, all crystallographic water molecules, co-crystallized ligands and heteroatoms were removed to prevent non-specific interactions. Structural quality and completeness of the channels were verified using PyMOL v2.5.4, ensuring no missing residues or distortions in the active or transmembrane domains. Polar hydrogens were added to improve electrostatic accuracy and hydrogen-bond prediction, while the proteins were converted into PDBQT format using the AutoDockTools (MGLTools) interface within PyRx v0.9.8. This conversion standardized atom types and prepared the receptors for docking compatibility with the AutoDock Vina algorithm.

Ligand selection and preparation

The principal phytochemical constituents of jasmine (*Jasminum sambac*) essential oil (α -pinene, benzyl acetate, linalool and phytosterols) were chosen for docking based on their frequent identification in GC–MS studies and reported neuroactive, anti-inflammatory and vasorelaxant properties.

The corresponding 3D ligand structures were retrieved from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov>) in SDF format using their compound identifiers (CIDs): phytosterols – 12303662; α -pinene – 6654; benzyl acetate – 8785; linalool – 6549. Ligands were imported into PyRx v0.9.8 using Open Babel v3.1.1, converted to PDBQT format and subjected to energy minimization with the MMFF94 force field to achieve geometrically stable conformations prior to docking.

Software validation

Molecular docking simulations were performed using AutoDock Vina integrated within PyRx v0.9.8 via the Vina Wizard interface. The molecular docking studies were performed using AutoDock Vina integrated within the PyRx v0.9.8 platform. The docking grid box was defined to cover the entire protein surface to enable comprehensive blind docking of ligands across all potential binding regions. The grid box dimensions were set to the maximum allowable size in PyRx (approximately $40 \times 40 \times 40$ Å), centered at the geometric midpoint of each protein structure. This configuration ensured unbiased ligand exploration and accurate identification of energetically favorable binding sites within the transmembrane and pore-forming domains of the sodium channel isoforms.

The reliability of the docking protocol was evaluated using RMSD (Root Mean Square Deviation) values obtained from the AutoDock Vina output within PyRx v0.9.8. For each ligand–protein complex, the top-ranked pose exhibited an RMSD value of 0.0 Å, indicating perfect self-consistency between the reference and docked

conformations. Subsequent poses displayed RMSD values ranging between 1.3 and 3.5 Å for most complexes, remaining within the acceptable range (<2.0–3.0 Å) recommended for reliable docking validation. This confirms that the generated docking poses were geometrically stable and accurately aligned within the predicted binding pocket. These RMSD outcomes validate the robustness of the docking pipeline and confirm that the conformational sampling performed by AutoDock Vina was both consistent and reproducible. Graphically presented in figures. 3 and 4.

Sodium Channel was docked with each ligand independently. Docking simulations were executed under identical parameters to ensure reproducibility. Their binding affinity values were recorded in kcal mol⁻¹. Root Mean Square deviation was used as the quality metric. The resulting Ligand and protein complexes were visualized in PyMOL and BIOVIA Discovery Studio Visualizer. High resolution, transparent, ray-traced images were produced via PyMOL and the final representable publications were generated via Microsoft PowerPoint and Adobe Photoshop.

Statistical analysis

The data were analyzed by SPSS version 23. Pearson's correlation coefficient was used to determine the association between the values of continuous variables. Values presented as mean \pm SD. Data was analysed using one-way ANOVA for intergroup comparisons and paired t-test for intragroup analysis and a statistically significant difference was considered $P < 0.005$.

RESULTS

Table 1 shows the demographic data of the participants. The participants of all three groups (group A, group B and group C) were divided on basis of gender, age, socio-economic background, quality of life, family history of cardiorespiratory diseases, marital status.

Table 2 shows the combined effect of electric foot massage with jasmine oil (group A), manual massage with jasmine oil (group B) and electric foot massage (group C) on cholesterol, respiration rate (RR), heart rate (HR), SBP, LDL, HDL and oxygen saturation. After the intervention, all the parameters were monitored and their values were analyzed. There was a significant decline in group A's cardiorespiratory parameters like SBP, RR and HR ($P = 0.000$) and an increase in oxygen saturation ($P = 0.000$). This effect is highly significant because of the combined effect of both jasmine oil and an electrical palm massager. There was a significant decline in levels of SBP, RR and HR ($P = 0.000$) and an increase in oxygen saturation ($P \leq 0.005$) in group B and insignificant results were obtained in group C ($P > 0.005$).

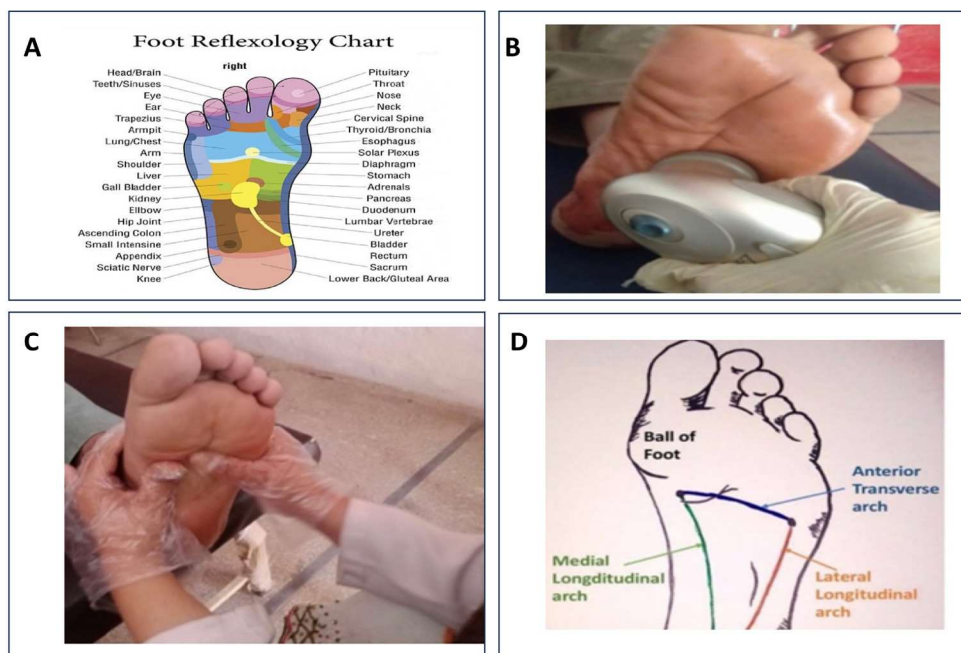


Fig. 2: (A) The tension points on the plantar surface of the foot; (B) Application of both the electrical massager and jasmine oil in traffic wardens suffering from stage 2 hypertension; (C) Manual massage of jasmine oil in traffic wardens suffering from stage 2 hypertension; (D) Anatomical position of tension points on the foot, cardiorespiratory pressure points present.

Table 1: Demographic characteristics of respondents.

	Group-A n (%)	Group-B n (%)	Group-C n (%)
<i>Gender</i>			
Male	65(67.01%)	50(52.083%)	49(51.041%)
Female	31(32.29%)	46(47.916%)	47(48.95%)
<i>Age</i>			
20-30 years	5(5.20%)	3(3.125%)	6(6.25%)
30-40 years	12(12.5%)	11(11.45%)	13(13.54%)
40-50 years	22(22.91%)	23(23.95%)	21 (21.875%)
50-60 years	26(27.083%)	33(34.375%)	26(27.08%)
60-70 years	31(32.29%)	26(27.0833%)	31(31.25%)
<i>Socioeconomic background</i>			
Rural	31(32.29%)	46(47.916%)	47(48.95%)
Urban	65(67.01%)	50(52.083%)	49(51.041%)
<i>Quality of life</i>			
Very poor	31.25%	28.29%	30.32%
Poor	22.91%	20.83%	22.91%
Neither			
poor nor good	18.75%	26.04%	20.83%
Good	16.66%	17.77%	15.63%
Very good	10.41%	6.251%	10.41%
<i>Family history of cardiorespiratory diseases</i>			
Yes	46(47.916%)	51(53.125 %)	26(27.083%)
No	50(52.083%)	45(46.875%)	70(72.91%)
<i>Marital status</i>			
Married	23(23.95%)	44(45.833%)	50(52.08 %)
Single	70(72.91%)	48(50%)	42(43.75%)
Widowed	3(3.125%)	2(2.083%)	1(1.041%)
Divorced	0(0%)	2(2.083%)	3(3.125%)

Table 2: Comparison of pre- and post-treatment values of parameters using paired t-test.

Parameters	Baseline Mean \pm S.D	After 3 weeks Mean \pm S.D	p-value (2-tailed)
<i>Group-A</i>			
Cholesterol (mmol/L)	2.69 \pm 0.73	0.93 \pm 0.51	0.001
LDL (mg/dL)	1.95 \pm 0.5	0.85 \pm 0.3	0.001
HDL (mg/dL)	1.01 \pm 0.25	1.66 \pm 0.25	0.001
Systolic pressure (mmHg)	151.73 \pm 25.93	122.46 \pm 7.08	0.001
Respiration rate (breaths/min)	21.00 \pm 3.60	16.67 \pm 1.01	0.001
Heart rate (beats/min)	79.33 \pm 5.13	64.01 \pm 2.01	0.001
Oxygen saturation (%)	95.33 \pm 1.15	98.01 \pm 0.57	0.001
<i>Group-B</i>			
Cholesterol (mmol/L)	2.60 \pm 0.73	2.47 \pm 0.64	0.005
Systolic pressure (mmHg)	150.92 \pm 25.01	144.08 \pm 17.06	0.001
LDL (mg/dL)	1.97 \pm 0.6	1.36 \pm 0.3	0.005
HDL (mg/dL)	1.00 \pm 0.25	1.25 \pm 0.22	0.005
Respiration rate (breaths/min)	22.00 \pm 3.72	21.89 \pm 2.75	0.001
Heart rate (beats/min)	77.86 \pm 5.13	71.01 \pm 4.17	0.005
Oxygen saturation (%)	96.00 \pm 1.07	97.01 \pm 1.04	0.005
<i>Group-C</i>			
Cholesterol (mmol/L)	2.71 \pm 0.82	2.60 \pm 0.73	0.008
Systolic pressure (mmHg)	152.83 \pm 26.01	141.63 \pm 16.08	0.006
LDL (mg/dL)	1.95 \pm 0.70	1.92 \pm 0.68	0.006
HDL (mg/dL)	1.03 \pm 0.26	1.11 \pm 0.25	0.008
Respiration rate (breaths/min)	20.15 \pm 2.67	20.00 \pm 2.54	0.010
Heart rate (beats/min)	78.01 \pm 6.01	74.12 \pm 4.02	0.006
Oxygen saturation (%)	96.01 \pm 1.07	96.10 \pm 1.06	0.008

HDL: High density cholesterol, LDL: Low density cholesterol, SBP: Systolic blood pressure, RR: Respiration rate, HR: Heart rate, SpO₂: Oxygen saturation

Table 3: One-way ANOVA for the comparison of cardiorespiratory and cardiometabolic parameters between three groups.

Parameters	Source	SS	Df	MS	F	p-value
Cholesterol	Between group	165.677	2	82.838	206.648	0.001
	Within group	114.247	285	0.401		
LDL	Between group	54.995	2	27.498	134.004	0.001
	Within group	58.482	285	0.205		
HDL	Between group	6.342	2	3.171	54.865	0.001
	Within group	16.473	285	0.058		
SBP	Between group	26,909.306	2	13,454.653	67.303	0.001
	Within group	56,974.958	285	199.912		
RR	Between group	1,341.101	2	670.550	133.805	0.001
	Within group	1,428.249	285	5.011		
HR	Between group	5,149.141	2	2,574.570	205.476	0.001
	Within group	3,570.993	285	12.530		
SpO ₂	Between group	175.238	2	87.619	103.892	0.001
	Within group	240.359	285	0.843		

HDL: High density cholesterol, LDL: Low density cholesterol, SBP: Systolic blood pressure, RR: Respiration rate, HR: Heart rate, SpO₂: Oxygen saturation

Table 4: Pearson correlation between objective parameters.

	Age	QOL	Health satisfaction	LDL mg/dL	HDL mg/dL	RR	Oxygen saturation	Systolic pressure
Age	1							
QOL	-0.97894	1						
Health satisfaction	-0.97894	1	1					
LDL	0	-0.05189	-0.051886249	1				
HDL	-0.9	0.808605	0.808604843	0.203069	1			
RR	-0.98346	0.967724	0.967724235	-0.17177	0.8686	1		
Oxygen Saturation	-0.27735	0.10644	0.106440263	0.168964	0.416025	0.231615	1	
Systolic pressure	0	-0.18566	-0.18566	-0.320135	0.2425	-0.0597	0.9417	1

Table 5: Binding affinity chart of Na^v1.7 (SCN09A), Na^v1.8 (SCN10A) and Na^v1.9 (SCN11A) with phytochemicals (α -pinene, benzyl acetate, linalool and phytosterols) and key interacting residues and bonds.

Sr.	Protein	Protein ID	Ligand	Ligand ID PubChem	Binding affinity	Key interacting residues and bonds
1.	Na ^v 1.7 (SCN09A)	6J8G PDB	Phytosterols	12303662	-10	TRP 1332, PHE 1748 (pi – sigma)
			Phytosterols		-9.5	CYS 1328, LEU 1329, LEC 1325, LEU 1400, LEC 1449, ILE 1745, PHE 1452 (pi – alkyl and alkyl)
			Phytosterols		-8.7	
			Phytosterols		-8.5	
			Phytosterols		-8.5	
			Phytosterols		-8.3	TYR 1396, ALA 1403, THR 1404 (Van der Waals)
			Phytosterols		-8.2	
			Phytosterols		-8.2	
2.	Na ^v 1.8 (SCN10A)	7WEL PDB	Phytosterols		-10.7	PHE 885, TYR 1717 (pi – sigma)
			Phytosterols		-10.4	LEU 1410, LEC 393, ILE 1418, ILE 1721, VAL 1414, VAL 1714, ILE 1718 (pi – alkyl and alkyl)
			Phytosterols		-10.3	
			Phytosterols		-10.1	
			Phytosterols		-9.8	
			Phytosterols		-9.3	LEU 1722, PHE 1725, LEU 882, LEC 889, THR 397, ILE 886, LEU 890 (Van der Waals)
			Phytosterols		-9.2	
			Phytosterols		-9.1	
3.	Na ^v 1.9 (SCN11A)	Q9UI33 AlphaFold	Phytosterols		-8.7	
			Phytosterols		-8.5	
			Phytosterols		-8.3	PHE 385, MET 1541, ILE 381, MET 1508, PHE 1545, LEC 1504 (pi – alkyl and alkyl)
			Phytosterols		-8.3	
			Phytosterols		-8.3	
			Phytosterols		-8.2	PHE 1505, GLY 1501, TYR 1599, PHE 1498, LEU 1494 (Van der Waals)
			Phytosterols		-8	
			Phytosterols		-7.8	
4.	Na ^v 1.7 (SCN9A)	-	Alpha-pinene	6654	-6.3	
			Alpha-pinene		-6.1	
			Alpha-pinene		-6	PHE 1446 (Pi – Sigma)
			Alpha-pinene		-5.7	PHE 921, ILE 1442, VAL 959, LEU 924, CYS 925, LEU 873, ILE 1441 (Pi – Alkyl and Alkyl)
			Alpha – pinene		-5.7	
			Alpha – pinene		-5.6	SER 1445, PHE 1405 (van der Waals)
			Alpha – pinene		-5.6	
			Alpha – pinene		-5.6	

Table. 5 is Continue....

Sr.	Protein	Protein ID	Ligand	Ligand ID PubChem	Binding affinity	Key interacting residues and bonds
5.	Na _v 1.8 (SCN10A)	-	Alpha – pinene		-5.9	PHE 1407 (pi - sigma) PHE 843, LEU 884, VAL 881, ILE 1403, LEU 846, LEU 794 (pi – alkyl and alkyl)
			Alpha – pinene		-5.9	
			Alpha – pinene		-5.8	
			Alpha – pinene		-5.8	
			Alpha – pinene		-5.7	
			Alpha – pinene		-5.6	
			Alpha – pinene		-5.6	
			Alpha – pinene		-5.6	
6.	Na _v 1.9 (SCN11A)	-	Alpha – pinene		-5.6	ILE 381, ILE 384, PHE 389, PHE 1545, LEU 1504 (pi – alkyl and alkyl) TYR 1599, PHE 385, SER 1548, THR 1549, GLY 1501 (Van der Waals)
			Alpha – pinene		-5.3	
			Alpha – pinene		-5.3	
			Alpha – pinene		-5.3	
			Alpha – pinene		-5.3	
			Alpha – pinene		-5.1	
			Alpha – pinene		-5.1	
			Alpha – pinene		-5	
7.	Na _v 1.7 (SCN9A)	-	Benzyl acetate	8785	-6.4	ARG 1613 (conventional hydrogen bond) ARG 1616, ALA 1615 (pi – alkyl) GLY 1592 (amide -pi – stacked) SER 1589, ILE 1555, ARG 1619, ASN 1551, TYR 1548, MET 1593 (Van der Waals)
			Benzyl acetate		-6.2	
			Benzyl acetate		-5.7	
			Benzyl acetate		-5.5	
			Benzyl acetate		-5.5	
			Benzyl acetate		-5.5	
8.	Na _v 1.8 (SCN10A)	-	Benzyl acetate		-5.8	SER 783 (conventional hydrogen bond) PHE (pi – pi stacked) LEU 794, PHE 843, LEU 884, THR 791, PHE 1408 (Van Der Waals)
			Benzyl acetate		-5.7	
			Benzyl acetate		-5.6	
			Benzyl acetate		-5.6	
			Benzyl acetate		-5.5	
			Benzyl acetate		-5.4	
			Benzyl acetate		-5.4	
			Benzyl acetate		-5.4	
9.	Na _v 1.9 (SCN11A)	-	Benzyl acetate		-5.8	ASN 1281, LYS 1203 (conventional hydrogen bond) PHE 1199 (pi – pi stacked) TYR 1287, PHE 1200, GLY 1284 (Van der Waals)
			Benzyl acetate		-5.8	
			Benzyl acetate		-5.8	
			Benzyl acetate		-5.5	
			Benzyl acetate		-5.5	
			Benzyl acetate		-5.3	
			Benzyl acetate		-5.2	
			Benzyl acetate		-5.2	
10.	Na _v 1.7 (SCN09A)	-	Linalool	6549	-5.3	PHE 963 (pi – sigma) LEU 398, LEU 964, ILE 1453, LEU 1449 (pi – alkyl and alkyl) ILE 1457, TYR 1755, ALA 399, ALA 402, ILE 1759, LEU 967 (Van der Waals)
			Linalool		-5.2	
			Linalool		-5.1	
			Linalool		-5.1	
			Linalool		-5	
			Linalool		-4.9	
			Linalool		-4.9	
			Linalool		-4.9	
Linalool	-4.8					

Table. 5 is Continue....

Sr.	Protein	Protein ID	Ligand	Ligand ID PubChem	Binding affinity	Key interacting residues and bonds
11.	Na _v 1.8 (SCN10A)	-	Linalool		-4.7	PHE 1619 (pi -sigma) PHE 1615 (pi - alkyl) MET 1267, PHE 1264, SER 1166, LEU 1616, ALA 1260, PRO 1257, SER 1166 (Van der Waals)
			Linalool		-4.7	
			Linalool		-4.6	
			Linalool		-4.6	
			Linalool		-4.5	
			Linalool		-4.5	
			Linalool		-4.5	
			Linalool		-4.4	
12.	Na _v 1.9 (SCN11A)	-	Linalool		-4.9	PHE 1199 (pi - sigma) LEU 1283, PHE 1200 (pi - alkyl and alkyl) LEU 1195, PHE 668, VAL 1290, ILE 1286, TYR 1287, ASN 1281, GLY 1284 (Van der Waals)
			Linalool		-4.9	
			Linalool		-4.8	
			Linalool		-4.8	
			Linalool		-4.8	
			Linalool		-4.8	
			Linalool		-4.7	
			Linalool		-4.6	

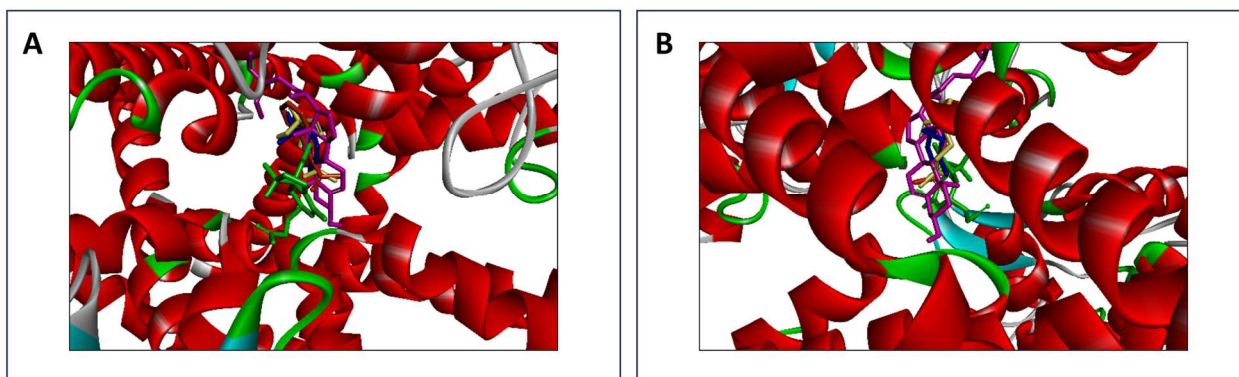


Fig. 3: (A-B) Superimposed complex of Na_v1.7, 1.8 native ligands with the ligand: alpha-pinene, linalool, benzyl acetate and phytosterols. The native ligand is shown in green. Phytosterol is presented in the pink, benzyl acetate is presented in the red color, linalool is presented in the yellow color and alpha-pinene is presented in the blue color.

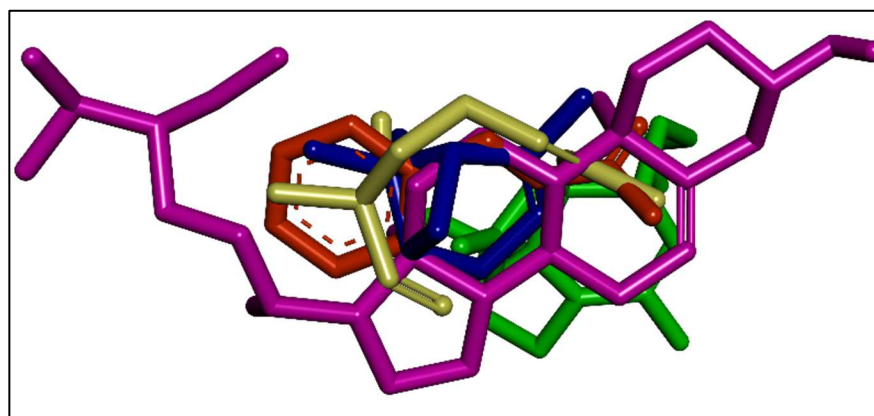


Fig. 4: Superimposed images of the native and our ligands. The native ligand is shown in green. Phytosterol is presented in the pink, benzyl acetate is presented in the red color, linalool is presented in the yellow color and alpha-pinene is presented in the blue color.

comparing cardiorespiratory and cardiometabolic parameters across three groups are shown in table 3. Overall, the ANOVA results indicate significant differences in all measured parameters (cholesterol, LDL, HDL, SBP, RR, HR and SpO₂) between the three groups.

Table 4 displays the correlation matrix for the variables under investigation. The correlation between the variables showed that HDL has good correlations with both QOL and health satisfaction, although age has a large negative correlation with both. Systolic pressure, oxygen saturation and respiratory rate all have correlations that shed light on how these variables relate to one another.

The docking results revealed variable binding affinities across sodium channel subtypes and ligands:

- *Phytosterols* demonstrated the strongest binding affinities among all tested ligands, with values reaching -10.7 kcal/mol for Na_v1.8 and -10 kcal/mol for Na_v1.7, indicating a high potential for blocking sodium channel activity. Their interaction likely involves multiple hydrophobic and Van der Waals contacts within the transmembrane domains (Table 5 (Sr. 1,2) Fig. 7 (D), Fig. 8 (D), Fig. 5 (D) and Fig. 6 (D)).
- *α -pinene* showed moderate binding, with the best docking score of -6.3 kcal/mol against Na_v1.7. This suggests it may possess mild channel-blocking properties, potentially contributing to analgesic or anti-inflammatory activity (Table 5 (Sr. 4) Fig. 5 (A), Fig. 6 (A)).
- *Benzyl acetate* exhibited relatively lower binding affinities, mostly ranging between -6.4 and -5.1 kcal/mol, suggesting weaker interaction with the sodium channels. However, the consistent binding across all three sodium channel types indicates a possible broad but mild modulatory effect (Table 5 (Sr. 7,8,9) Fig. 5 (C), Fig. 6(C), Fig. 7(C), Fig. 8(C), Fig. 9 (C) and Fig. 10 (C)).
- *Linalool* also showed lower docking scores -5.3 to -4.4 kcal/mol, but stable RMSD values suggest it docks in similar conformations across different channel types. This supports linalool's known mild analgesic properties, possibly via partial sodium channel modulation (Table 5 (Sr. 10,11,12) Fig. 5 (B), Fig. 6(B), Fig. 7(B), Fig. 8(B), Fig. 9(B) and Fig. 10(B)).

In general, Na_v1.8 exhibited slightly better binding across most ligands compared to Na_v1.7 and Na_v1.9, suggesting that this isoform may offer a more favorable binding pocket for phytochemicals.

DISCUSSION

Many flowers around the world have phytochemical compositions of therapeutic importance. Out of these flowers, we have used *J. sambac's* oil. Numerous studies have documented its biological activities (Khan *et al.*,

2021). Naturally, there are tension points of body organs under the foot (plantar surface). These tension points can be stimulated through the foot's reflexology mechanism, which generates a biological response. We have used electrical massagers and manual massage techniques to stimulate the desired trigger points, leading to organ responses (Biswas *et al.*, 2022). By pressing on the tension points of the heart and kidneys in the medial arch of the plantar surface (Fig. 1), many heart parameters can be changed. Previous research has also demonstrated the impact of foot massage on heart rate and blood pressure in 30 patients admitted to the coronary care center and among traffic wardens suffering from stage 2 hypertension (Dike and Desmond, 2022). According to Jin Shin Jyutsu Theory, this touch's intricacies could release energy blockages, thereby increasing mechanical characteristics in the body (Kilicli and Zeyneloglu, 2024).

A foot massage is a type of cutaneous sensory input that can help the body reach homeostasis by changing the way blood flows to the tissues around the edges. Vasomotor activity happens outside of the body during foot massage, which relaxes smooth muscles and widens blood vessels. Massage is widely recognized as a form of relaxation that relieves fatigue by decreasing sympathetic nervous system activity, thereby lowering blood pressure and improving circulation (Smith, 2020). When you rub down on vagus nerve fibers, they release acetylcholine, which comes close to nodal cells and lowers the frequency of depolarization. This makes your heart beat slower. A reduction in heart rate results in prolonged ventricular filling and increased stroke volume and cardiac output. An increase in cardiac output can increase circulation throughout the body, including the respiratory system, likely resulting in a balanced exchange of carbon dioxide and oxygen. The oxygen saturation will increase while the levels of oxygen and carbon dioxide in the tissue remain the same. The stimulation at the center of breathing is intended to slow the breathing rate (Perwasha *et al.*, 2022). In our study, using both Jasmine oil and an electrical massager together significantly lowered cholesterol, LDL, HDL, SBP and HR (Table 2). This could be because the antioxidants in jasmine oil, which include ascorbic acid and flavonoids, work well with the deep kneading Shiatsu technique of an electric massager. This is because the Shiatsu technique improves circulation and blood flow, which helps muscles heal faster and reduces inflammation, as shown in other antioxidant studies (Khan *et al.*, 2021; 2022; Mizgan *et al.*, 2022).

Through stimulation, reflexology can assist in opening blocked energy pathways by repeatedly applying pressure and manipulating nerve endings (Smith, 2020). Foot reflexology is a treatment based on the principle that there are specific points on the feet that correspond to various organs, glands and systems in the body.

Docking of Na_v1.8 with Phytochemicals

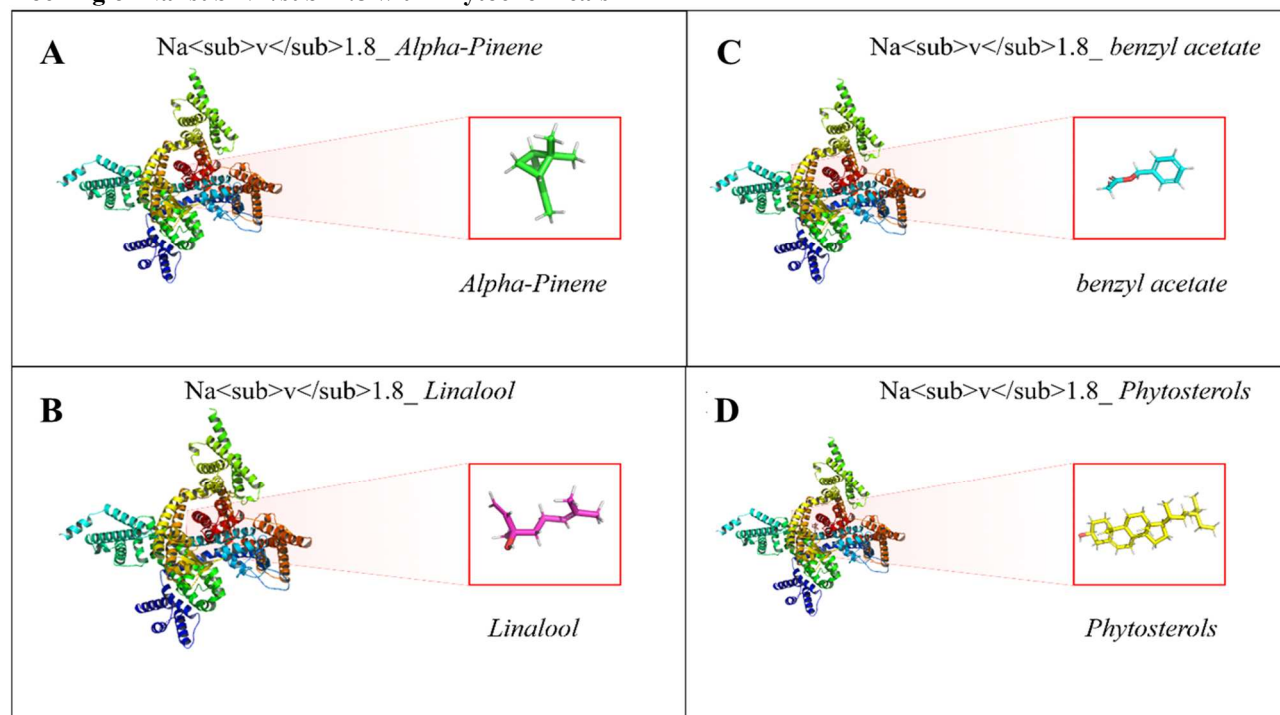


Fig. 7: 3D complex interaction of the Na_v1.8 with the ligand; (A) interaction with alpha-pinene; (B) interaction with linalool; (C) interaction with benzyl acetate; (D) interaction with phytosterols.

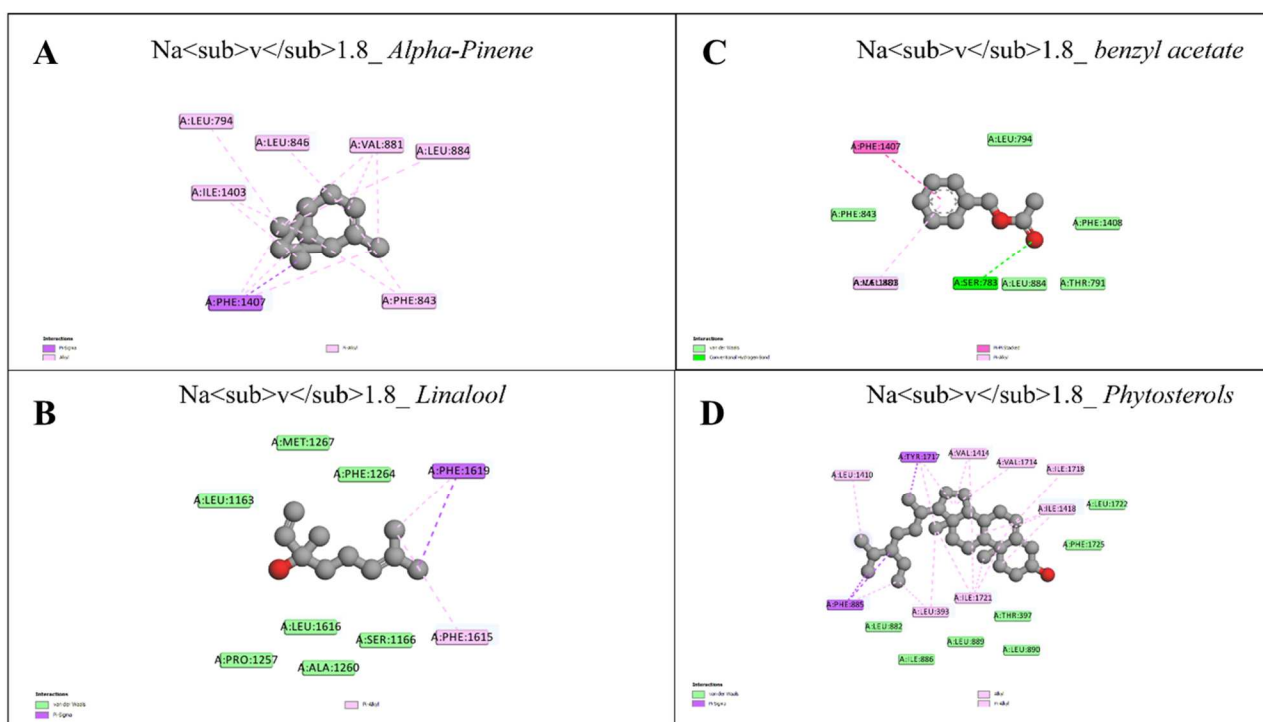


Fig. 8: 2D interaction chart of the Na_v1.8 with the ligand; (A) interaction with alpha-pinene; (B) interaction with linalool; (C) interaction with benzyl acetate; (D) interaction with phytosterols. In this figure, light green color represents Van der Waals, dark green color represents the conventional hydrogen bond, purple color represents pi-sigma bond and light and dark pink represent pi-alkyl and alkyl bonds.

Docking of Na_v1.9 with Phytochemicals

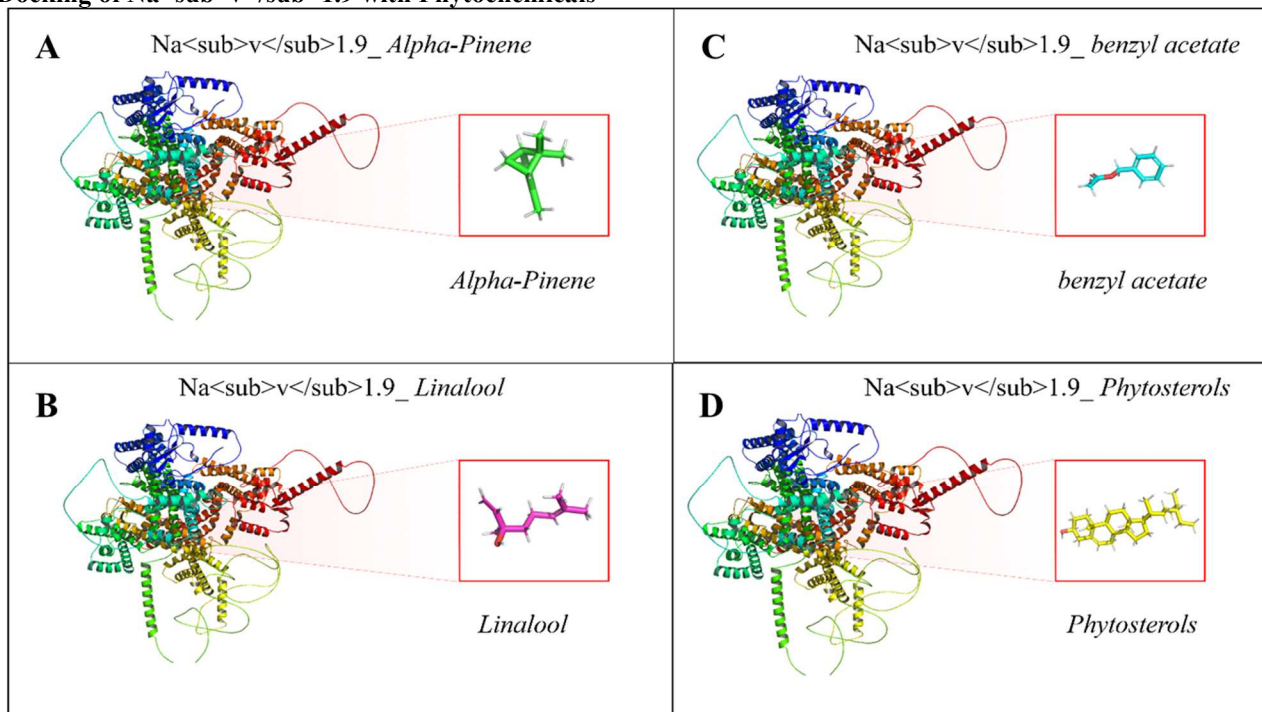


Fig. 9: 3D complex interaction of the Na_v1.8 with the ligand; (A) interaction with alpha-pinene; (B) interaction with linalool; (C) interaction with benzyl acetate; (D) interaction with phytosterols.

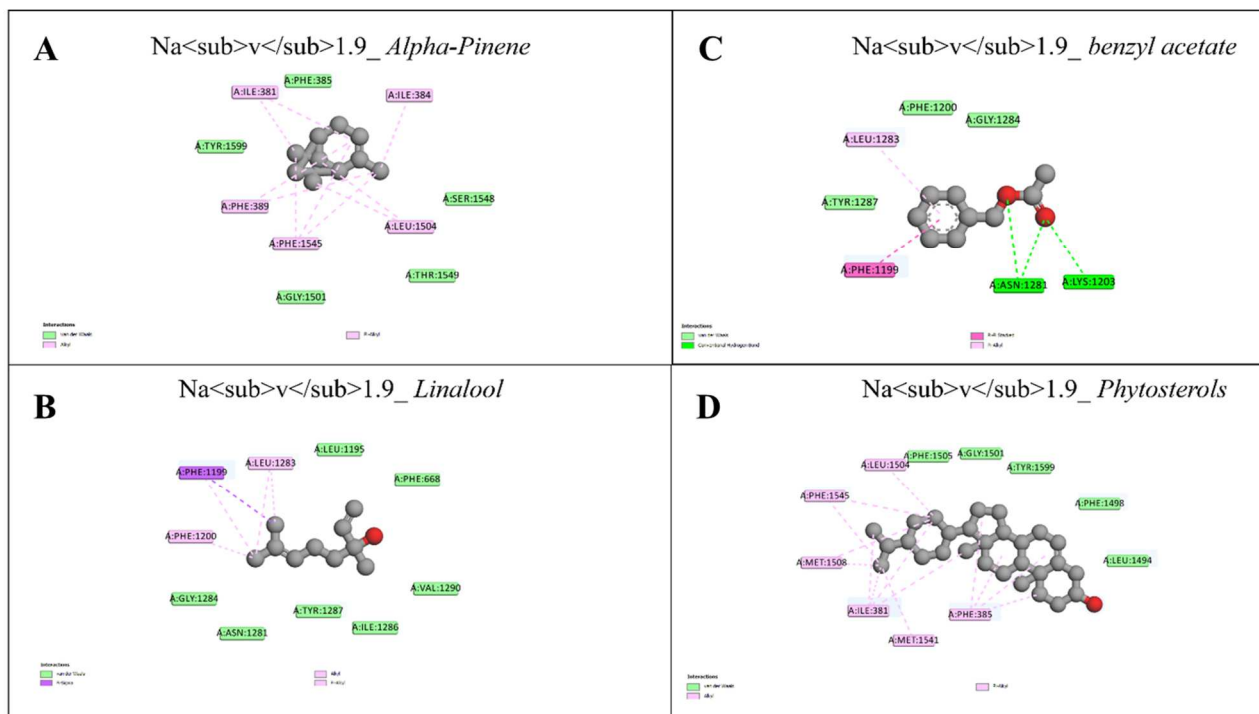


Fig. 10: 2D interaction chart of the Na_v1.9 with the ligand; (A) interaction with alpha-pinene; (B) interaction with linalool; (C) interaction with benzyl acetate; (D) interaction with phytosterols. In this figure, light green color represents Van der Waals, dark green color represents the conventional hydrogen bond, purple color represents pi-sigma bond and light and dark pink represent pi-alkyl and alkyl bonds.

Reflexology applies targeted pressure and manipulates these reflex points to restore balance, enhance circulation and allow the natural flow of energy throughout the body. This holistic approach is believed to stimulate the nervous system, relieve stress and promote overall well-being. A wide range of health benefits, from pain relief and better sleep to management of conditions like anxiety, headaches and digestive issues, have been attributed to regular sessions of foot reflexology (Kiliçli and Zeyneloglu, 2024). It has even been widely used as a complementary therapy in integrative health care because it poses no harm and can support both physical and emotional health. While scientific evidence is mixed, many practitioners and reflexology recipients report significant improvements in relaxation and overall health. Reflexology allegedly achieves this by modifying the flow of nerve impulses, nutrients and blood (Kilicli and Zeyneloglu, 2024). An "action potential" is an electrical current that cells emit. Sensory nerves carry this electrical current to the brain, which relays it to nearby muscles and organs, triggering a reaction (Table 2). Ultimately, this enhances general wellness. In previous years, many studies have highlighted the therapeutic effects of jasmine oil and massage techniques. No study has highlighted the combined effects of jasmine oil and electrical massage techniques, which can increase drug absorption and improve therapeutic effects.

Phytosterols exhibited the highest binding affinities, with scores of -10.7 kcal/mol for Na_v1.8 and -10 kcal/mol for Na_v1.7 (Table 5 (Sr. 2,1) Fig. 7(D), Fig. 8(D), Fig. 5(D), Fig. 6(D)). This indicates that phytosterols have a strong potential for blocking sodium channel activity, which is key for therapeutic applications in pain, hypertension and other disorders where sodium channel activity is implicated. Interaction profiling revealed extensive hydrophobic and π - σ contacts with residues such as TRP 1332, PHE 1748, CYS 1328, LEU 1329, ILE 1745 and PHE 1452 in Na_v1.7 and PHE 885, TYR 1717, LEU 1410, ILE 1418 and VAL 1414 in Na_v1.8. These residues form π - π , π - σ and alkyl interactions that stabilize the ligand deep within the hydrophobic transmembrane pocket. The additional van der Waals contacts with residues such as TYR 1396, ALA 1403, THR 1404, LEU 1722 and PHE 1725 contribute to conformational complementarity. Collectively, these interactions explain the high docking scores and support previous evidence that phytosterols can mediate smooth muscle relaxation by modulating ion channel activity (Anjos *et al.*, 2013).

α -pinene had a moderate docking score of -6.3 kcal/mol against Na_v1.7 (Table 5 (Sr. 4) Fig. 5(A), Fig. 6(A)). The ligand formed a π - σ interaction with PHE 1446 and several hydrophobic (π -alkyl and alkyl) contacts with PHE 921, ILE 1442, VAL 959, LEU 924, CYS 925, LEU 873 and ILE 1441, while SER 1445 and

PHE 1405 contributed van der Waals stabilization. These findings indicate that α -pinene can occupy a peripheral hydrophobic pocket of the sodium channel, conferring mild inhibitory potential. This aligns with its known bioactivity as an antihypertensive and lipid-lowering compound through vascular modulation and LDL reduction (Mohamed *et al.*, 2021).

The docking scores for benzyl acetate ranged from -6.4 to -5.1 kcal/mol. The relatively weak binding affinity suggests that benzyl acetate has a less potent effect in blocking sodium channels compared to phytosterols (Table 5 (Sr. 7,8,9) Fig. 5(C), Fig. 6(C), Fig. 7(C), Fig. 8(C), Fig. 9(C) and Fig. 10 (C)). However, its consistent binding across all three sodium channel isoforms (Na_v1.7, Na_v1.8, Na_v1.9) suggests that it may have a broad, but mild, modulatory effect. Phytosterols and benzyl acetate demonstrated consistent interaction across all sodium channel isoforms (Na_v1.7, Na_v1.8, Na_v1.9). Key hydrogen bonds with ARG 1613 (Na_v1.7) and SER 783 (Na_v1.8) stabilized the ligand orientation, while π - π stacking with PHE 1199 and π -alkyl interactions with ARG 1616, ALA 1615, LEU 794 and PHE 843 enhanced hydrophobic complementarity. The network of van der Waals interactions involving TYR 1287, GLY 1592, ASN 1551 and MET 1593 further contributed to complex stabilization. This could be useful in therapies requiring less intense sodium channel inhibition or for conditions where a mild, broad modulation of channel activity is beneficial; it is well reported to be a stress modulator by inhibiting cortisol production (McCord and Kaufman, 2017).

Linalool displayed binding scores ranging from -5.3 to -4.4 kcal/mol, which is on the lower end compared to the other ligands. Linalool's relatively lower affinity, paired with stable RMSD values, suggests that while it might not be a strong blocker, it still consistently interacts with sodium channels in a similar conformation (Table 5 (Sr. 10,11,12) Fig. 5(B), Fig. 6(B), Fig. 7(B), Fig. 8(B), Fig. 9(B) and Fig. 10(B)). Although its affinity was comparatively lower, linalool formed stable contacts across the sodium channel isoforms, primarily through π - σ and hydrophobic interactions. In Na_v1.7, the ligand interacted with PHE 963, LEU 398, LEU 964, ILE 1453 and LEU 1449 (π - σ and alkyl), supported by van der Waals interactions with ILE 1457, TYR 1755 and ALA 399. Similar interactions were observed for Na_v1.8 and Na_v1.9, involving PHE 1619, PHE 1264, LEU 1616 and PHE 1199 residues. These consistent hydrophobic and van der Waals contacts imply a stable but weak interaction profile. The modest binding of linalool corresponds with its pharmacological role as a mild analgesic and vasodilator, acting through

partial sodium channel inhibition and nitric-oxide-mediated vascular relaxation (Khan *et al.*, 2024).

This study has limitations that should be considered when interpreting the findings. The first limitation is that the study was conducted at a single center, which may limit the generalizability of the results to traffic wardens in other regions or professionals in different occupational settings. Despite these constraints, the study provides practical recommendations to enhance the well-being of traffic wardens and other occupational groups who face similar risks in the workplace. The treatment procedure could be part of workplace health interventions, such as massaging sessions during scheduled breaks, the availability of massagers and basic oils at home, or even a wellness center in the organizational compound. Such measures could help reduce the health problems associated with prolonged standing and the management of highly stressful situations, without causing significant access problems or disruptions to working hours. These practical applications emphasize the requirement for larger multicenter trials to validate the approach and support broader implementation.

CONCLUSION

According to this study, deep-tissue foot massage with jasmine essential oil or an electric massager can help lower blood pressure and other health parameters, possibly by modulating voltage-gated sodium channels and HDL. It especially helps reduce stress in traffic cops with stage 2 hypertension. These findings suggest introducing such interventions into occupational health programs to address the unique challenges traffic wardens and similar professionals face in their workplaces. Workplaces could interpret this by incorporating massage protocols into regular wellness initiatives for employees, perhaps providing on-site massage services during breaks or portable massagers and essential oils for at-home use. It could help mitigate the adverse effects of prolonged standing and job-related stress, ultimately enhancing the quality of life and productivity of workers in risk-prone jobs. Large-scale, multi-center trials should guide future studies to validate these findings and evaluate the feasibility of scaling up such interventions in diverse settings. Also, more advanced experimental methods should be used to elucidate the mechanisms underlying these therapies so we can better understand how they help people. These steps would lead to evidence-based guidelines for occupational health management that are broadly applicable and long-term in impact.

Acknowledgments

The authors are grateful to the management of Muhammad Institute of Medical and Allied Sciences, Multan, for providing research facilities.

Authors' contributions

Imran Ahmad Khan: Study design; Nadeem Ahmad: Phytochemical analysis; Mudassar Yasin: Data analysis; Maliha Khalid Khan and Ujala Hameed: Clinical trial; Sarmad Frogh Arshad: Developed *in-silico* experiment; Qasim Ali Ghauri: Performed *in-silico* experiments; Qurat Ul Ain: Manuscript writing and literature review; Hasan Riaz: Reviewed literature and wrote the manuscript

Funding

There was no funding.

Data availability statement

Data will be available on request.

Ethical approval

All the experiments were approved by the Institutional Ethical Review Board (IRB No. MIMAS/03/26/IAK). The clinical trial was registered in a WHO-recognized clinical trial registry (IRCT20230103057033N2). The Helsinki Declaration was followed for research involving humans. This study was performed in adherence with the CONSORT guidelines. See supplementary file for the CONSORT checklist.

Conflict of interest

The authors declare no conflict of interest.

Supplementary data

<https://www.pjps.pk/uploads/2026/06/SUP1781433209.pdf>

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