Pharmacogn. Res., 2027; 19(2):839-847.
https://www.phcogres.com

Original Article

Interpreting *Trivrit Avaleha*'s Multi-Component, Multi-Target Mechanisms in Bronchial Asthma: A GC-MS-Guided Computational Pharmacology Investigation

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ABSTRACT

Background: The symptoms of bronchial asthma, a chronic inflammatory airway disease, include coughing, wheezing, dyspnea, and reversible airflow restriction. Even if traditional medication efficiently reduces symptoms, long-term usage is frequently linked to negative side effects, which calls for the investigation of safer treatment options. Although its molecular mechanism is still poorly understood, *Trivrit Avaleha*, a traditional Ayurvedic formulation mostly including *Operculina turpethum*, has been used to treat *Tamaka Swasa* (bronchial asthma). **Objectives:** To identify the phytochemical constituents of *Trivrit Avaleha* using Gas Chromatography-Mass Spectrometry (GC-MS) and elucidate its probable molecular mechanism against bronchial asthma through computational pharmacology and molecular docking. **Materials and Methods:** To identify the phytochemicals in *Trivrit Avaleha*, GC-MS analysis was performed. ADMETLab 3.0 and Swiss Target Prediction were used to screen the compounds that were found. GeneCards and the Human Protein Atlas were used to obtain targets linked to bronchial asthma, and Venny 2.1.0 was used to do an overlap analysis. Using STRING, Cytoscape, and DAVID Bioinformatics, protein-protein interaction, hub gene identification, and KEGG pathway enrichment analyses were carried out. Using PyRx, molecular docking against important hub targets was used to further assess important phytochemicals. **Results:** Twenty phytochemicals were found by GC-MS analysis, with 5-hydroxymethylfurfural, 1-oleoyl-2-palmitoylglycerol, palmitic acid vinyl ester, eugenol, and benzoic acid being notable components. 64 common targets were found by computational pharmacology; hub genes included BCL2, HIF1A, EGFR, ESR1, and STAT3. Pathways in Cancer, Metabolic Pathways, Lipid and Atherosclerosis, and Neuroactive Ligand-Receptor Interaction pathways were all significantly involved, according to KEGG enrichment. Eugenol showed the highest binding affinity among the phytochemicals, especially toward STAT3 (-6.1 kcal/mol) and BCL2 (-5.9 kcal/mol), according to molecular docking, which supports its possible anti-inflammatory effect. **Conclusion:** Through a multi-component, multi-target mechanism of action encompassing important inflammatory and apoptotic pathways, the current study offers preliminary mechanistic data supporting *Trivrit Avaleha* therapeutic promise against bronchial asthma. These results provide a scientific foundation for its traditional Ayurvedic use and call, for additional *in vitro, in vivo*, and clinical research to confirm its pharmacological effectiveness.

Keywords: Bronchial asthma, *In silico*, *In vitro*, Trivrit avaleha.

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Received: 08-06-2026;
Revised: 23-08-2026;
Accepted: 18-10-2026.

INTRODUCTION

A chronic inflammatory illness of the airways, bronchial asthma is characterized by repeated episodes of wheezing, dyspnoea, chest tightness, and coughing, often at night or in the early morning, as well as fluctuating airflow restriction and bronchial hyperresponsiveness. The illness causes reversible bronchoconstriction and chronic airway inflammation as a result of intricate interactions between environmental factors and genetic predisposition (Lee *et al.*, 2018). Exposure to allergens (house dust mites, pollen, animal dander, Molds), respiratory virus infections, tobacco smoke, air pollution, occupational irritants, exercise, cold air, obesity, emotional stress, and some drugs (such as aspirin and non-selective β-blockers) are common causes. A significant global health issue, asthma affects around 260 million people globally and is responsible for almost 420,000

DOI: 10.5530/pres.20270286

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fatalities each year (Goldin & Cataletto, 2026). Although it varies by age, location, and diagnostic criteria, the prevalence in India is between 3.4% and 6% (Bhalla *et al*., 2018).

In order to obtain the best possible symptom control and avoid exacerbations, bronchial asthma is currently managed pharmacologically using a stepwise approach that combines controller and relief drugs. Long-acting β_2-agonists (LABAs) like formoterol or salmeterol are often used in conjunction with Inhaled Corticosteroids (ICS) like budesonide and fluticasone, which constitute the cornerstone of long-term therapy (Gauvreau *et al*., 2014). While leukotriene receptor antagonists (like montelukast), long-acting muscarinic antagonists (like tiotropium), oral corticosteroids, and biologic agents are only used in certain patients with severe or persistent disease, Short-Acting β_2-Agonists (SABAs), like salbutamol, offer quick relief during acute attacks (Normansell *et al*., 2016). Despite their efficacy, these drugs can have side effects like oral candidiasis and dysphonia with ICS, tremor, tachycardia, and hypokalemia with β_2-agonists, headache and neuropsychiatric effects with montelukast, dry mouth with anticholinergics, weight gain, hyperglycemia, osteoporosis, hypertension, and adrenal suppression with prolonged systemic corticosteroid use (Aggarwal, 2016). These drawbacks highlight the need for safer and more potent treatment options for managing asthma.

In Ayurveda, Bronchial asthma can be co-related with *Tamaka swasa*, the premonitory symptoms of Bronchial asthma is as similar as *Tamaka swasa*. In these aspects, the treatment protocol for the disease is *Virechana* (purgation). Among the purgative agents, the plant *Operculina turpenthum* (*Trivrit*) is the one drug of choice, the plant is either given directly given as *Churna* (Powder) or else as *Avaleha* (Linctus) form. According to *Charaka Samhita*, a major classical treatise in Ayurveda, the *Trivrut avaleha* is prepared with the root of the plant by adding honey and sugar to it (Sharma & Dash, 2009). Moreover according to *Sharangadhara Samhita*, it is also considered as a drug of choice in *Virechana*, as the *Shresta Dravya* (Best medicine) for inducing purgation (Sharangadharacharya, 2005) The plant *Operculina turpethum* is having not only analgesic activity, hepato-protective activity but also anti-inflammatory activity and anti-bacterial activity (Kim *et al*., 2023).

Although, the plant as a single drug has been studied in all pharmacological aspects but the linctus separate chemical quantification hasn't been performed to establish the mode of action. Moreover, the disease bronchial asthma is especially chosen here as the main treatment protocol in *Ayurvedic* perspective is purgation. With the chemical quantification of the *Trivrit avaleha* (Herbal linctus) and analysing the mode of action in the Bronchial asthma not only validates the formulation but also explains the mechanism of action.

MATERIALS AND METHODS

Firstly, the *Trivrit avaleha* was procured from Vaidya Ratnam GMP certified with batch number 25C2280, followed by that the GCMS analysis was done with Ethyl acetate. Here, ethyl acetate was chosen as solvent because of the intermediate polarity, which enables the efficient extraction of a broad range of volatile and semi-volatile constituents while minimizing the co-extraction of highly polar matrix such as sugars, proteins and polysaccharides. *Trivrit avaleha*, contains many compounds such as phenolics, flavonoids, anthraquinones and triterpenoids, hence due to the prevalence of these compounds' ethyl acetate was considered for GCMS profiling. The methodology outline is given in the Figure 1.

Ethical statement

The study didn't require ethical approval because it didn't include human subjects, animals, or experimental methodologies derived from animals. The Institutional Ethics Committee (IEC) and the Institutional Animal Ethics Committee (IAEC) approval wasn't required.

GCMS

The test material was precisely weighed at 100 mg and diluted in 20 mL of ethyl acetate. The solution was filtered through a 0.22 µm PTFE syringe filter into a GC vial after being vortexed and sonicated for 10 to 15 min to guarantee total dissolution. The sample was further diluted with ethyl acetate if necessary to achieve an appropriate concentration for analysis. A Shimadzu GCMS-QP8040 Gas Chromatography-Mass Spectrometer with an AOC-20i Auto Injector was used to examine the prepared sample. An SH-Rxi-5Sil MS capillary column (30 m × 0.25 mm i.d., 0.25 µm film thickness; 5% biphenyl, 95% dimethyl polysiloxane) was used for the chromatographic separation process. The sample was injected in splitless mode using a 1 µL aliquot while the injector temperature was kept at 250°C. At a steady flow rate of 1.0 mL/min, helium served as the carrier gas. The oven ran for 53 min total, starting at 50°C and rising at a pace of 10°C per minute to 310°C, where it remained for 25 min. Electron Ionization (EI) at 70 eV was used in the Q3 scan mode of the mass spectrometer. The temperature of the ion source, interface, and detector were all kept at 230°C, 250°C, and 0.2 kV, respectively. GCMSsolution software was used to process the chromatograms and mass spectra, and by comparing the resultant mass spectra with those found in the NIST Mass Spectral Library, the compounds were tentatively identified.

Computational pharmacology

The phytochemicals that were quantified in the GCMS was taken for the computational studies, firstly the chemical compounds were put into PubChem for discovering the SMILES (Simplified Molecular Input Line Entry System) (Kim *et al*., 2023), followed

by that the ADMET analysis was done using ADMET Lab 3.0. Lipinski rule of 5, Drug likeliness, Blood Brain Barrier, Respiratory toxicity and Human Intestinal Absorption (Dong *et al.*, 2024). After assessing these parameters, the phytochemicals were filtered and the targets related to phytochemicals were predicted with Swiss Target Prediction (Daina *et al.*, 2019). The targets related to the disease were procured from two databases namely Genecards and Human Protein Atlas, the duplicates were removed and the targets were organised and uploaded into Venny 2.1.0. The plant targets were also uploaded into Venny 2.1.0 and the common targets were predicted (Safran *et al.*, 2021; Uhlén *et al.*, 2015; Oliveros, 2007) With the overlapping targets uploaded into STRING 11.0, the protein interaction was made and top 10 genes were predicted with Cytohubba in Cytoscape 3.10.4. (Szklarczyk *et al.*, 2023; Shannon *et al.*, 2003). The common targets were further uploaded into DAVID bioinformatics for prediction of Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway (Chin *et al.*, 2014). The top 10 were organised based on the ranking of one to ten, followed by this the topological analysis of pathway-target-chemicals were performed to construct a network in Cytoscape 3.10.4.

Molecular docking

With the top 3 targets and the chemical structures that are available in the topological analysis, the docking was performed by downloading the 3D structures from PubChem. The targets 3D structures were downloaded from RCSB PDB, with the Autodock tool 1.5.7, Kollman charges and Hydrogen bonds were added (Sherman *et al.*, 2022; Dallakyan & Olson, 2015). Later with PyRx the docking of the targets and phytochemical was performed to assess the binding affinity of the molecules (Morris *et al.*, 2009). Followed by this the 2D and 3D visualisation of the docked molecules were done in Biovia 2025 to assess the hydrogen bonds and other structures of the target and ligand (Biovia, 2025).

RESULTS

The GCMS analysis of *Trivrit avaleha* identified a total of 20 compounds including furan derivatives, fatty acids, phenolics, organic acids and fatty acid esters. The main components found were 1-oleoyl-2-palmitoylglycerol (11.35%), 5-hydroxymethylfurfural (34.56%), 4H-pyran-4-one derivative (10.06%), 1,2,3-propanetriol 1-acetate (8.67%), and palmitic acid vinyl ester (7.09%). In Table 1, the GCMS results are tabulated with peak number, retention time, identified compound and area %. The GCMS peak is given in Figure 2, the peak, area, retention time and the identified compound are given in Table 1.

Plant targets and Overlapping targets

The phytochemicals related to the formulations were uploaded into PubChem for searching the SMILES, after this the SMILES were uploaded into ADMET Lab 3.0 for ADMET analysis with Lipinski rule of 5, Drug likeliness with less than 0.67 as cut off score, Human Intestinal Absorption as 0.5 as a cut off score and Respiratory toxicity as 0.5. With the cut off scores a total of 3 phytochemicals were obtained. The SMILES of these chemicals were uploaded into Swiss Target Prediction for further target analysis that are related to these phytochemicals. With the targets obtained from Gene cards and HPA both were merged and duplicates were removed and a total of 6209 targets were available, after filtering the targets with a cut off score of 5, a total of 896 targets were available for "Bronchial asthma". Both the plant and disease targets were uploaded into Venny 2.1.0 and a total of 64

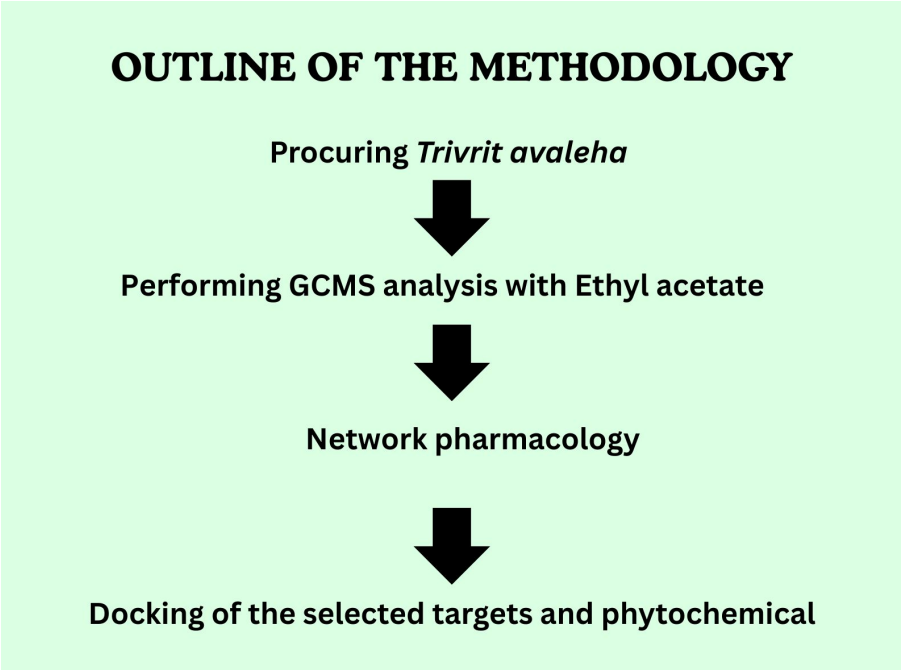

Figure 1: Methodology outline.

Table 1: GCMS analysis and the peak number, Retention time, Compound and Area % of *Trivrit avaleha*.

Peak No.	RT (min)	Identified Compound	Area (%)
1	3.854	2-Furanmethanol	0.86
2	7.511	Methyl 2-furoate	0.42
3	8.584	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl	10.06
4	9.126	Benzoic acid	2.16
5	10.028	5-Hydroxymethylfurfural	34.56
6	10.281	1,2,3-Propanetriol, 1-acetate	8.67
7	11.172	Glutaric acid, dec-2-yl geranyl ester	1.82
8	11.300	Eugenol	0.63
9	14.548	2-Cyclopenten-1-one, 4-butyl-3-methoxy	4.26
10	14.850	Tricyclo [3.3.1.1(3,7)] decane derivative	0.36
11	18.216	n-Hexadecanoic acid	1.36
12	19.865	cis-9-Hexadecenal	1.28
13	20.070	Octadecanoic acid	0.44
14	34.812	Octadecanoic acid, 3- [(1- oxohexadecyl) oxy]-2-hydroxypropyl ester	1.76
15	38.338	Eicosanoic acid, 2- [(1- oxohexadecyl) oxy]-1-[(octadecanoyl)oxy] ethyl ester	2.40
16	38.848	Palmitic acid vinyl ester	7.09
17	44.036	1-Oleoyl-2-palmitoylglycerol	11.35
18	44.623	Octadecanoic acid, ethenyl ester	4.34
19	50.900	9-Octadecenoic acid (Z)-, 2-hydroxy-3-[(1-oxohexadecyl) oxy] propyl ester	3.74
20	51.953	2-Nonanol oleate	2.45

common targets were retrieved. The overlapping targets are given in Figure 3.

Protein interaction, Top 10 gene prediction and KEGG pathway prediction

The common targets were further uploaded into STRING 11.0 for observing the protein interaction, among this PTGS2, BCL2, STAT3 and EGFR had the most interaction between other targets. And in the top 10 gene prediction the cytohubba predicted that, BCL2, HIF1A, EGFR, ESR1, STAT3, PARP1, PPARG, EP300, RELA and HSP90AA1 were the 10 genes among the 64 common targets. With common targets, further uploaded into DAVID Bioinformatics the KEGG pathway was predicted and a total of 99 pathways was found. Among these the top 10 pathways were taken to further topological analysis, the pathways included metabolic pathways, cancer pathways, lipid and atherosclerosis and neuroactive ligand-receptor interaction pathway. The top 10 pathways were selected on the basis of the gene count present in each pathway. The protein interaction, top 10 genes are given in the Figure 4.

Topological analysis & Molecular docking

The pathway - target - chemicals were merged to form a network in which the targets such as BCL2, HIF1A, EGFR had the most degree layout while the targets with lesser interactions had the least degree layout. With the targets and the chemicals docking was performed in PyRx, Salbutamol was also taken for docking as a standard modern drug. The docking was performed for the phytochemicals such as Eugenol, Benzoic acid, Salbutamol and 2-Cyclopenten-1-one, 4-butyl-3-methoxy- towards targets HIF1A, STAT3, EGFR and BCL2. Among this Salbutamol had the highest binding affinity towards STAT3 with a docking score of -6.8 kcal/mol, while among the phytochemicals in the formulation i.e. eugenol had the highest docking affinity towards -6.1 kcal/mol towards STAT3. On checking the average binding affinity, the phytochemical eugenol had the highest among the all-other phytochemicals in the formulation, although salbutamol had shown highest in comparison with other phytochemicals in all the other target, In BCL2 Eugenol had highest binding affinity when compared to Salbutamol. The lowest docking score was for 2-Cyclopenten-1-one, 4-butyl-3-methoxy- towards HIF1A with a score of -4.0 kcal/mol. The 2D and 3D visualisation of the docking is given in Figure 6, while the topological analysis of *Trivrit avaleha* is given in Figure 5, binding affinity of targets towards phytochemical is given in (Table 2 and Figure 6).

DISCUSSION

The *Trivrit* (*Operculinia turpethum*) as drug has *Tikta* & *Madhura rasa, Ushna veerya* and *Katu vipaka* (Bitter in taste, Hot in potency and Pungent in post-digestive effect). With these properties, the

plant in *Ayurvedic* treatise has properties that cure *Swasa* and *Kasa* (Respiratory disorders) (Gupta *et al.*, 2017). *Tikta rasa* is having *Krimighna* (Anti-bacterial and Anti-microbial) action, *Kleda upasoshana* (dries up excessive mucus) and *Katu rasa* (spice taste) is having *marga vivarnoti* (clears the channels) and dries up the excessive mucous. *Ushna veerya* (Hot potency) directly helps in the activity of purgation, and moreover the *mahabhuta* [predominance of elements should be *Prithvi* (Soil) and *Jala* (Water)]. In this, *Tikta rasa* is having predominance of *Prithvi* (Soil) and *Vayu* (Air), which makes the drug i.e. *Operculina turpethum* as a major drug in purgation. Thus, making it a direct drug of choice in the respiratory disorder, furthermore it is also having purgative action which is essential for treatment of Bronchial asthma (Bhavamishra *et al.*, 2013; Narahari *et al.*, 2010).

With the chemical quantification of the *Trivrit avaleha*, it will furthermore validate the ancient wisdom with current modern parameters. Followed by that predicting the mechanism of action will additionally validate the use of the linctus in bronchial asthma. One naturally occurring derivative of benzoic acid that shows promise in treating allergic asthma is hydroxybenzoic acid. Hydroxybenzoic acid dramatically decreased perivascular and peribronchial inflammatory cell infiltration and inhibited IL-5 production in an ovalbumin-induced mouse model, suggesting decreased eosinophilic airway inflammation. Serum IgE, IL-4, and IL-13 levels were not considerably changed, indicating a specific mechanism of action as opposed to widespread immunosuppression. Peroxybenzoic acid, on the other hand, did not exhibit any appreciable protective properties. The anti-inflammatory characteristics of benzoic acid are probably caused by the hydroxyl group that is connected to its structure. Although more preclinical and clinical research is needed to determine its molecular targets, efficacy, and safety, these results point to hydroxybenzoic acid as a possible lead molecule for creating tailored treatments for allergic asthma (Makoui *et al.*, 2025).

A significant bioactive component of cloves (*Syzygium aromaticum*), eugenol (4-allyl-2-methoxyphenol) has garnered a lot of interest due to its strong anti-inflammatory and antioxidant qualities. According to the reviewed data, eugenol inhibits the expression of inflammatory mediators like COX-2 and iNOS, suppresses the activation of NF-κB, and reduces the production of pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6. Furthermore, by raising the activities of Glutathione (GSH), Catalase (CAT), and Superoxide Dismutase (SOD) while lowering Reactive Oxygen Species (ROS), eugenol strengthens endogenous antioxidant defenses. Eugenol's potential as a promising natural therapeutic agent for inflammatory respiratory illnesses, including bronchial asthma, is further supported by experimental investigations that show it reduces leukocyte

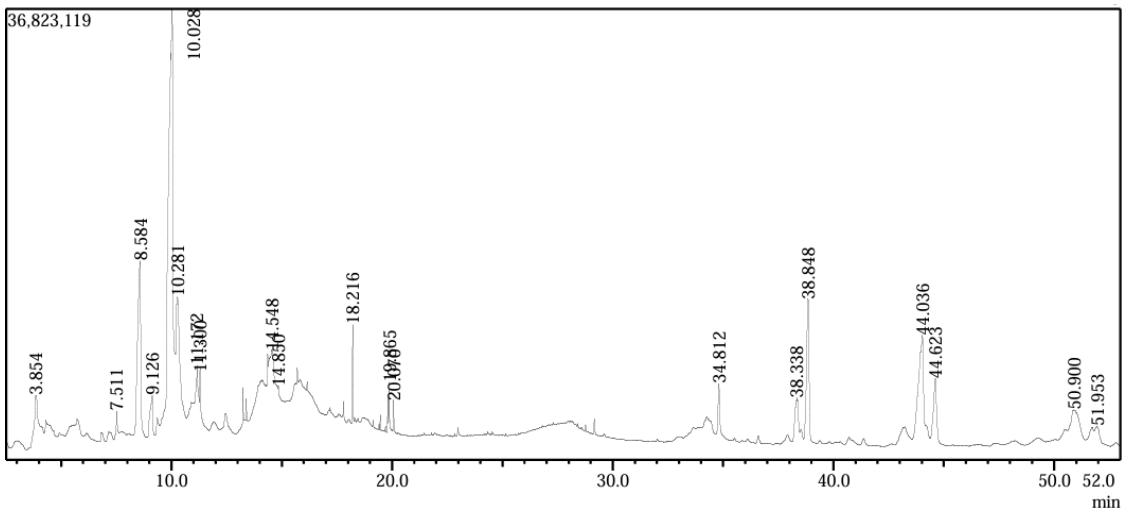

Figure 2: GCMS peak area.

Table 2: Binding affinity of targets and phytochemicals.

	Binding affinity of targets and Phytochemicals (kcal/mol)				
Phytochemical	**Targets**	**HIF1A**	**EGFR**	**STAT3**	**BCL2**
	PDB ID	**1qlb**	**2gs60**	**6njs**	**4ieh**
Salbutamol		-6.1	-6.1	-6.8	-5.7
2-Cyclopenten-1-one, 4-butyl-3-methoxy-		-4.0	-5.0	-5.6	-5.4
Eugenol		-4.9	-5.3	-6.1	-5.9
Benzoic acid		-4.6	-5.0	-5.5	-5.4

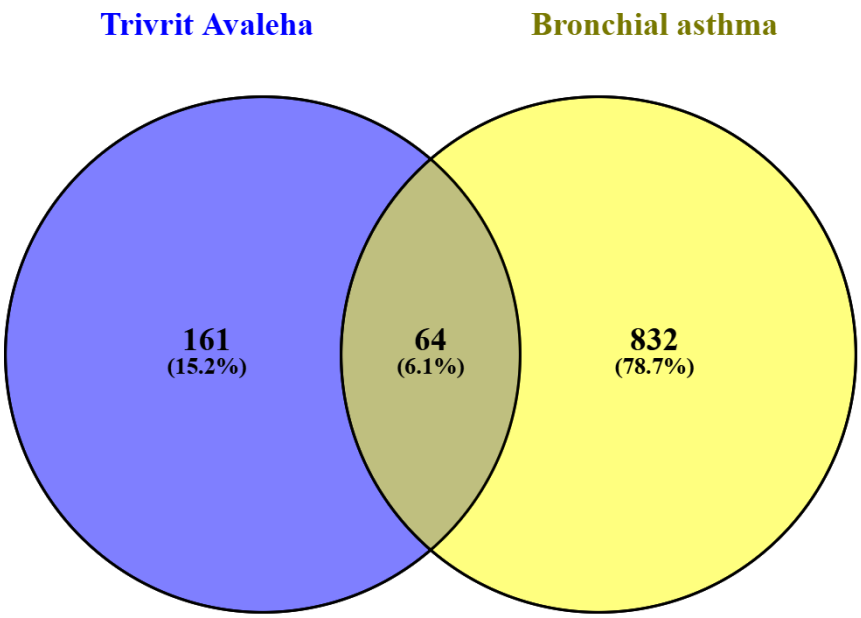

Figure 3: Overlapping targets - Trivrit avaleha.

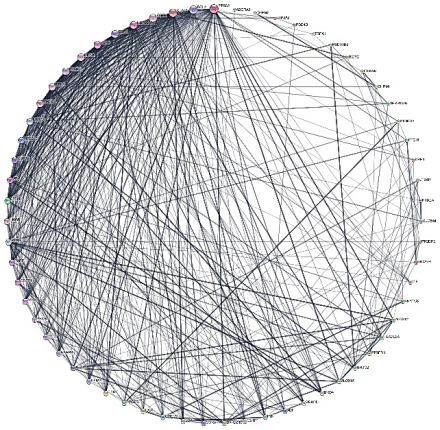

Figure 4: PPI - Trivrit avaleha.

infiltration, attenuates lung inflammation, and maintains pulmonary architecture (Damasceno *et al.*, 2024).

A crucial transcription factor in the pathophysiology of bronchial asthma, STAT3 (Signal Transducer and Activator of Transcription 3) controls immune cell activation, cytokine signalling, and airway inflammation. When the JAK/STAT3 signalling pathway is activated, Th2 and Th17 cells differentiate, M2 macrophages polarize, and airway epithelial and endothelial cells become activated. This leads to an increase in the production of pro-inflammatory cytokines and chemokines. This contributes to airway remodelling, mucus hypersecretion, eosinophilic and neutrophilic infiltration, and hyperresponsiveness. Selective inhibition of STAT3 significantly lowers lung inflammation and enhances airway function, according to experimental research, making STAT3 a prospective therapeutic target for both steroid-resistant and eosinophilic forms of bronchial asthma. Developing new anti-asthmatic treatments may be aided by modifying STAT3 signalling (Nikolskii *et al.*, 2021).

In Respiratory illnesses like bronchial asthma, where epithelial cell apoptosis and airway remodelling contribute to disease progression, the function of Bcl-2 in controlling apoptosis is equally pertinent. According to the review, Bcl-2 is an essential anti-apoptotic protein that prevents caspase activation and programmed cell death by maintaining the integrity of the mitochondrial membrane and blocking the release of Cytochrome C. While increasing expression of pro-apoptotic proteins like Bax encourages mitochondrial malfunction and cell death, decreased expression of Bcl-2 increases the apoptosis of airway epithelial cells, resulting in tissue damage and persistent inflammation. Bcl-2 is therefore a possible therapeutic target in chronic inflammatory airway illnesses since preserving the equilibrium between Bcl-2 and Bax is essential for controlling apoptosis,

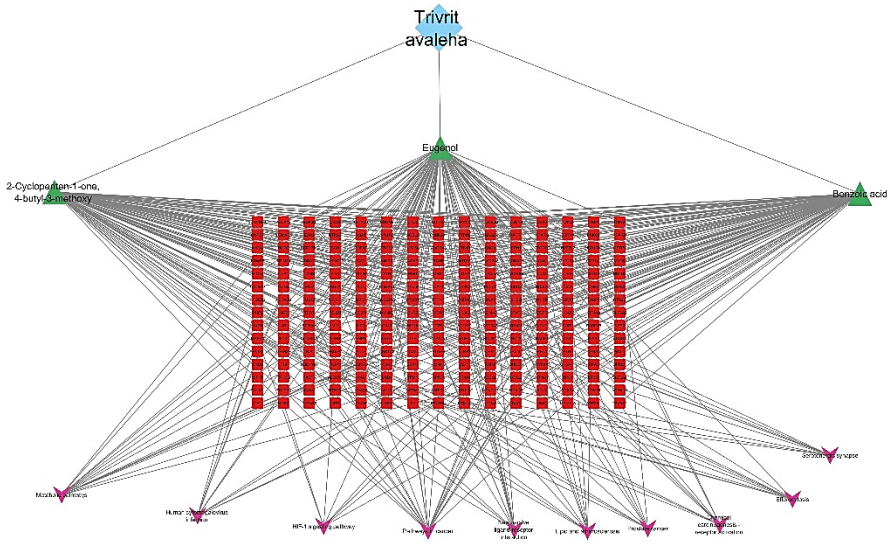

Figure 5: Topological analysis - Trivrit avaleha.

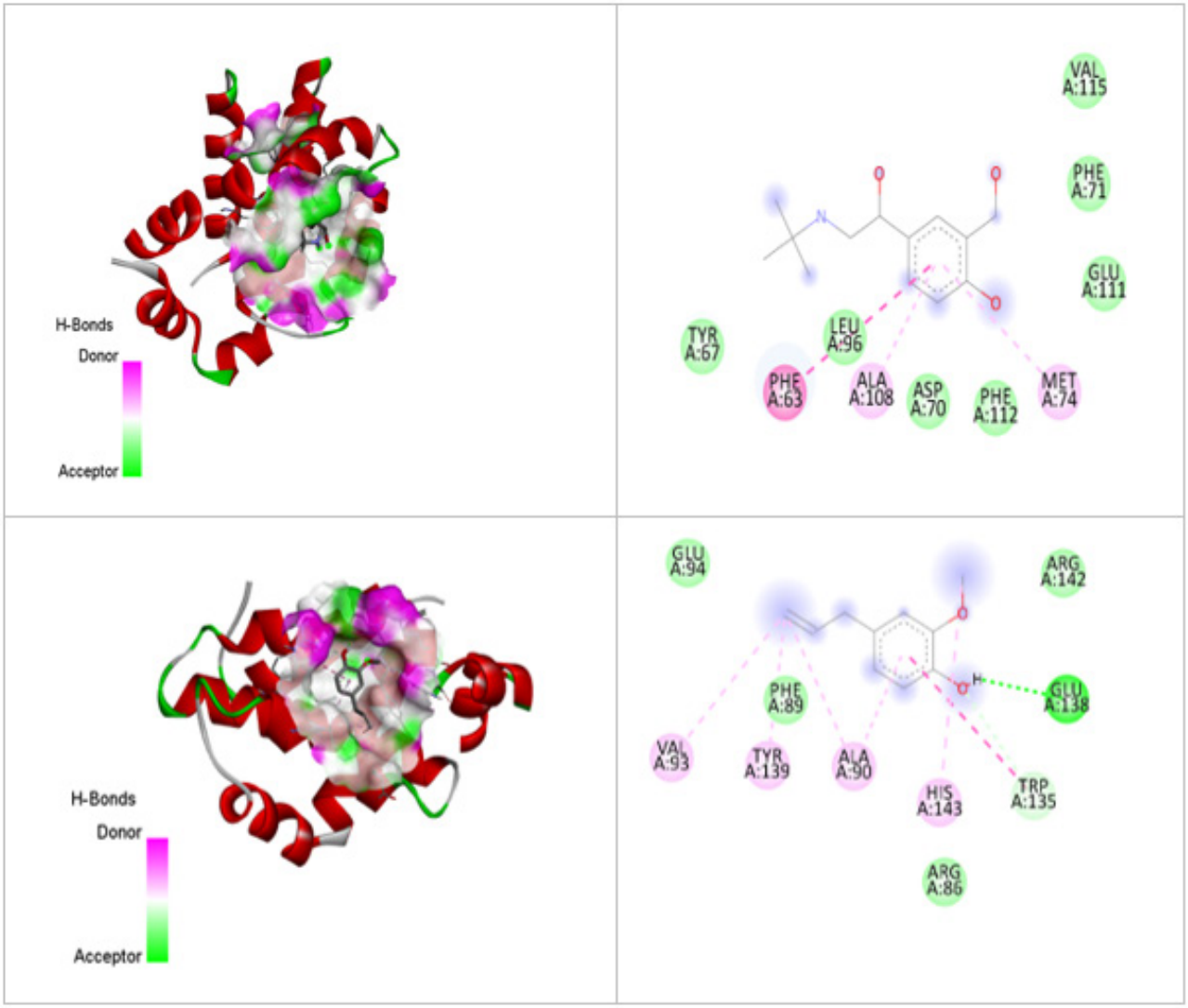

Figure 6: Docking visualization.

safeguarding airway structural cells, and reducing inflammatory damage (Zeng *et al*., 2012).

The "Pathways in cancer" KEGG pathway was shown to be one of the highly enriched signalling pathways linked to the molecular mechanisms that lung cancer and asthma share. Numerous oncogenic and inflammatory signalling cascades, such as PI3K/Akt, MAPK, JAK/STAT, NF-KB, TGF-β, and p53, are integrated into this system (Sanchez-Vega *et al*., 2018). These cascades control angiogenesis, cell proliferation, apoptosis, immunological responses, and tissue remodelling. Dysregulation of these pathways increases vulnerability to airway remodelling and may be connected to lung carcinogenesis by causing oxidative stress, aberrant cell survival, persistent airway inflammation, and epithelial damage. Targeting these similar signalling networks may offer new asthma treatment approaches while lowering the risk of lung cancer progression, according to the enrichment of the "Pathways in cancer" pathway, which emphasizes the connection between inflammatory and tumorigenic pathways (Zhou *et al*., 2025).

Overall, the docking analysis suggests that the ligand occupies the active site effectively and interacts with several amino acids through the complementary non-covalent interactions. The presence of hydrogen bonds together with extensive hydrophobic and aromatic nature of the ligand suggests that binding affinity of the ligand and target is comparatively high and the structural stability. Moreover, the Eugenol towards BCL2 targets is comparatively on the higher side when compared with salbutamol suggesting the mechanism of *Trivrit avaleha* towards BCL2 is comparatively higher.

Although the study has predicted the mechanism of the herbal formulation, there are few limitations in the study, the disease targets that are procured and the analysis of the phytochemicals were performed in the databases which are having regular update and only screening of few hundreds to thousand targets were only done in the disease databases, which becomes a bias. Henceforth, a complete *in vitro* and *in vivo*, followed by that a clinical trial will evaluate the mechanism of *Trivrit avaleha* in bronchial asthma.

CONCLUSION

When a medicine is used in a wrong dose or manner or with any other combination it acts as a poison meanwhile if a poison is used in a correct manner or a dose then it will act as a medicine. (Sharma *et al*., 2009). Without knowing a plant or formulation's mechanism administering to a patient may cause a trouble for both the doctor and a patient. Thus, understanding a formulations mechanism is must and should.

With this intention the study was performed and it was prophesied that phytochemicals such as eugenol and benzoic acid were found to be binding with targets such as BCL2 and STAT3 in pathways such as Metabolic pathway and Pathways in cancer. Although, the study has given the preliminary evidence regarding the mode of action, a pre-clinical and clinical trial will validate the role of *Trivrit avaleha* in *Tamaka swasa* (Bronchial asthma).

ABBREVIATIONS

LABA: Long-acting β_2-agonists; **IMPPAT:** Indian Medicinal Plant, Phytochemistry and Therapeutics; **KEGG:** Kyoto Encyclopaedia of Genes and Genomes; **ADME:** Absorption, Distribution, Metabolism and Excretion; **PPI:** Protein-Protein Interaction; **HPA:** Human Protein Atlas; **RCSB PDB:** Research Collaboratory for Structural Bioinformatics Protein Data Bank; **Rf:** Retention factor; **SMILES:** Simplified Molecular Input Line Entry System; **SABA:** Short-Acting β_2-Agonists; **GC-MS:** Gas Chromatography-Mass Spectrometry.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Cite this article: Chavan SG, Gramapurohit P, Singh S, Naik BRM. Interpreting *Trivrit Avaleha's* Multi-Component, Multi-Target Mechanisms in Bronchial Asthma: A GC-MS-Guided Computational Pharmacology Investigation. Pharmacog Res. 2027;19(2):839-47.