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## Research Paper

# Analyzing potential phyto-constituents from *Acalypha indica* Linn (Haritamanjari) in management of Asthma: computational approach

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## ABSTRACT

Background and Aim: Asthma is a major global health concern, necessitating the exploration of natural alternative to synthetic drugs due to their side effects. This study investigates the anti-asthmatic potential of *Acalypha indica* Linn through in-silico molecular docking. Material and Methods: Six phytoconstituents from *Acalypha indica* Linn and standard drugs used as anti-asthmatic agents were selected. Molecular docking was performed using AutoDock 4.5.6 against key asthmatic targets including, PDE4B, M3 receptor, IL-13, and ALOX. Interactions were visualized using Biovia discovery studio. Result: The phytoconstituents exhibited higher binding affinities with target proteins compared to standard drugs. Notably, Stigmasterol, Aurantiamide, and Kaempferol showed strong interactions with PDE4B, with binding energies of -12.00, -9.78, and -6.53 kcal/mol, respectively, surpassing Theophylline's -4.98 kcal/mol. For the M3 muscarinic receptor Aurantiamide, Acalyphin, and Kaempferol demonstrated binding energies of -10.68, -7.09, and -6.55 kcal/mol, outperforming Ipratropium bromide's -8.48 kcal/mol. Stigmasterol, and Aurantiamide exhibited robust binding with the IL-13, with energies of -7.47, and -6.37 kcal/mol, respectively, compared to Fluticasone's -5.93 kcal/mol. Additionally, Stigmasterol, Aurantiamide, and Caffeic acid interacted strongly with the ALOX5, with binding energies of -10.53, -8.41, and -6.27 kcal/mol, respectively, exceeding Montekulast's -9.14 kcal/mol. Conclusion: This research highlights the therapeutic potential of *Acalypha indica* Linn in management of asthma, offering a promising alternative to synthetic drugs. The findings support further experimental validation and clinical application, paving the way for novel anti-asthmatic drug discovery.

## INTRODUCTION

Asthma is a chronic respiratory condition characterized by inflammation and narrowing of the airways, leading to symptoms such as

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wheezing, coughing, dyspnea, and chest tightness. Affecting over 262 million people globally as of 2019, asthma remains a significant public health concern with increasing prevalence, particularly among children and adolescents [1, 2]. The disease is multifactorial in origin, involving genetic predisposition, environmental triggers, and immune dysregulation. Key pathological features include epithelial damage, airways smooth muscle hypertrophy, hypersecretion of mucus, and heightened responsiveness to allergens or irritants [1]. Advances in understanding asthma pathogenesis have highlighted the central role of airway epithelium and immune responses, paving the way for novel therapeutic approaches targeting inflammation and structural changes rather than merely alleviating symptoms [3, 4]. Despite progress in treatment modalities such as inhaled corticosteroids and biological agents, asthma management continues to face challenges due to its heterogeneity and complex underlying mechanism [1, 4]. This underscores the need for innovative strategies, including phytomedicine and computational approaches, to identify effective interventions for this debilitating condition. Asthma is a chronic inflammatory disorder of the airways characterized by bronchoconstriction, airway hyperresponsiveness, and excessive mucus production [5]. The pathophysiology involves complex interactions between immune cells, inflammatory mediators, and structural airway components [5, 6]. Proteins such as PDE4B, M3 receptor, IL-13, and ALOX play pivotal roles in driving these pathological changes. PDE4B contributes to inflammation by regulating cyclic AMP levels, which enhances immune cell activation and cytokine release. The M3 receptor, a subtype of muscarinic receptors, mediates bronchoconstriction through acetylcholine-induced smooth muscle contraction [7]. IL-13, a cytokine primarily secreted by Th2 cells, promotes mucus hypersecretion,

airway remodeling, and eosinophilic inflammation [5]. ALOX, involved in leukotriene synthesis, amplifying inflammatory processes and bronchial hyperreactivity [6, 7]. Together, these molecular pathways exacerbate airway narrowing and obstruction, forming the hallmark features of asthma [8]. Existing pharmaceutical approaches for mitigating asthma encompass various drugs. These drugs are effective but show a variety of adverse effects. Theophylline, Ipratropium bromide, Fluticasone and Montelukast are widely used in asthma management but are associated with various adverse effects. Theophylline may cause nausea, vomiting, headache, insomnia, and serious complications such as seizures and cardiac arrhythmias [9, 10]. Ipratropium bromide, an anticholinergic agent, can lead to dry mouth, blurred vision, urinary retention, headache, and rarely paradoxical bronchospasm. Fluticasone, a corticosteroid, linked to oral thrush, hoarseness, sore throat, adrenal suppression, osteoporosis with long-term use, and increased susceptibility to infections. Montelukast is generally well-tolerated but may cause headache, abdominal pain, fatigue, and in rare cases, mood changes like depression or suicidal thoughts [11]. While these drugs are effective in controlling asthma symptoms, their potential side effects necessitate careful monitoring during treatment. This emphasizes the necessity for drug development focused on medication with negligible adverse effects. Consequently, herbal remedies, with their diverse pharmacological activities and generally safer profiles, offer promising alternatives. *Acalypha indica* Linn has been utilized in traditional medicine for centuries due to its diverse pharmacological activities, including its efficacy as a bronchodilator [12]. *Acalypha indica*, belonging to the Euphorbiaceae family, is an erect herb widely distributed across tropical and subtropical regions of Asia, Africa, and South America. Known for its diverse pharmacological



properties, the plants has been extensively utilized in traditional medicine systems such as Ayurveda, Siddha, and Unani. In this study, we aim to explore the molecular interactions between phytoconstituents of *Acalypha indica* Linn (Haritamanjari) and marketed drugs with key proteins associated with asthma. This approach not only provides insights into the potential mechanism underlying the anti-asthmatic effects of *Acalypha indica* Linn, but also supports the integration of traditional herbal remedies into modern therapeutic strategies for management of asthma. Our aim is to identify potential therapeutic agents with reduced side effects compared to current standard drugs utilized in asthma. This approach may lead to the development of novel, safer therapeutic agents derived from plant source.

## 1. MATERIALS AND METHODS

### 1.1. Data Collection and Structure Retrievals:

An exhaustive literature review was conducted for identify the phytochemicals in *Acalypha indica* Linn and standard drugs which is used for asthma. The 3D structures of selected phytochemicals were retrieved from PubChem database (<https://pubchem.ncbi.nlm.nih.gov>).

Additionally, the 3D structure of selected target proteins, including Phosphodiesterase 4B (PDE4B) (PDB ID: 3WWE), Muscarinic-3 receptor (PDB ID: 8E9W), IL-13 (PDB ID: 5L6Y), Lipo-oxygenase (ALOX) (PDB ID: 7TTK) were obtained from Protein Data Bank (PDB) [<https://www.rcsb.org>] [13].

**1.2. ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) and Drug related Properties:** The drug likeness, bioavailability scores and ADME (Absorption, Distribution, Metabolism, and Excretion) profiles of the phytoconstituents were evaluated using the Swiss ADME tool

(<http://www.swissadme.ch>) [14]. Toxicity prediction for the compounds were performed via the ProTox-II web server ([https://tox-new.charite.de/protox\\_II](https://tox-new.charite.de/protox_II)) [15].

**Molecular docking analysis:** Confirmational energy stabilization of the phytochemicals was conducted using the Avogadro tool (<https://avogadro.cc>) [16]. Molecular interactions between target proteins and ligands were analysed via AutoDock 4.2 and AutoDock Tools 1.5.6 (<http://www.scripps.edu/mb/olson/doc/autodock>). Protein preparation included the removal of water molecules, co-crystallized ligands, and non-essential heteroatoms using UCSF Chimera [17]. Subsequently, the processed proteins were imported into AutoDock Tool (v1.5.6) for addition of polar hydrogen atoms, assignment of Kollman charges, and configuration of atom types as AD4. A grid box, cantered on the active site, was spatially optimized using the DeepSite tool (<https://www.playmolecule.com/deepsite>) to define docking coordinates. The study assessed ligand-protein binding mechanisms through molecular docking, with resultant complexes visualized in Biovia Discovery Studio for detailed analysis of 2D and 3D interactions patterns.

## 2. RESULT

**2.1. Screening of phytochemicals and Potential targets:** Phytoconstituents were systematically identified via a comprehensive literature survey. Bioactive candidates underwent preliminary screening using drug-likeness ( $\geq 0.18$ ) and oral bioavailability ( $\geq 30\%$ ) thresholds, culminating in six prioritized compounds (Table 1). These underwent multi-parametric evaluation,



encompassing drug likeness (as depicted in Table 2), pharmacokinetic profiling (ADME parameters in Table 3), toxicological assessment (Table 4), and computational docking simulations.

**2.2. Molecular Docking:** Molecular docking simulations were conducted using AutoDock version 4.5.6 to evaluate the interactions between phytoconstituents and asthma-related proteins. The study aimed to identify optimal binding conformations, with more negative binding energy indicating stronger binding affinity. Binding energies below 0 kcal/mol were considered favorable, and values below -6 kcal/mol indicated strong binding interactions. Visualization of the best docking poses in both 2D and 3D formats revealed significant results. Phytoconstituents demonstrated superior binding interactions compared to standard drugs with amino acid residues, as shown in Table 5. For instance, Stigmasterol, Aurantiamide, and Kaempferol exhibited high affinities with PDE4B at -12.00, -9.78, and -6.53 kcal/mol, respectively, surpassing Theophylline's -4.98 kcal/mol. Similarly, Aurantiamide, Acalyphin, and Kaempferol showed robust binding with the M3 muscarinic receptor at -10.68, -7.09, and -6.55 kcal/mol, outperforming Ipratropium bromide's affinity of -8.48 kcal/mol. Further analysis highlighted Stigmasterol and Aurantiamide's strong interactions with IL-13 at -7.47 and -6.37 kcal/mol, respectively, compared to Fluticasone's affinity of -5.93 kcal/mol. Additionally, Stigmasterol, Aurantiamide, and Caffeic acid demonstrated high binding energies with ALOX at -10.53, -8.41, and -6.27 kcal/mol, respectively, while Montelukast showed a lower affinity of -9.14 kcal/mol (Table 5). These findings underscore the therapeutic potential of phytoconstituents

as effective alternatives for asthma treatment by exhibiting stronger binding interactions with key target proteins than conventional drugs.

**3.3. Heatmap Generation:** The binding affinity scores of ligands interacting with potential targets were systematically compiled into a data matrix. This matrix was analyzed using R programming (version 4.2.3), and the findings were represented as a heatmap, as depicted in Figure 2. In this heatmap, a color gradient ranging from red to blue indicates the range of binding energies, where blue indicates high and red signifies low binding affinities.

## 4. DISCUSSION

Asthma, a chronic inflammatory disorder of the airways, is marked by bronchial hyperresponsiveness, reversible airflow obstruction, and immune-mediated inflammation involving cytokines, mast cells, and airway remodelling [18-20]. Despite advancements in pharmacotherapy, existing treatments often face limitations such as systemic side effects and incomplete symptom control, necessitating novel therapeutic strategies. Traditional medicinal plants like *Acalypha indica* Linn have garnered attention for their multi-target potential, particularly given their historical use in respiratory ailments [12]. This study highlights the molecular interactions of six phyto-constituents including, Stigmasterol, Aurantiamide, Acalyphin, Gallic Acid, Caffeic Acid, and Kaempferol with key asthma-related targets, offering insights into their synergistic roles in bronchial relaxation and inflammation modulation. The identification of these bioactive compounds of *Acalypha indica* Linn was conducted through comprehensive literature review. Subsequently, the SwissADME tool was employed to evaluate oral bioavailability (OB), drug-likeness (DL), and ADME properties which



facilitated the phytochemical selection. Protox-II web server was utilized for toxicity estimation. Additionally, target proteins associated with asthma were selected. AutoDock4 tool was employed to conduct molecular docking studies aimed to analyzing the interactions between the selected phytochemicals and the targeted proteins. The consequence shows that all compounds exhibited promising binding affinities with the targeted proteins. Remarkably, Stigmasterol, Aurantiamide, Acalyphin, Gallic acid, Caffeic acid and Kaempferol exhibited significant binding energies with target proteins, including PDE4B, M3 receptor, IL-13, and ALOX. These interactions may promote broncho-dilation, which contribute to the therapeutic efficacy of *Acalypha indica* Linn in managing asthma. Literature shows that several phyto-constituents demonstrate promising biological relevance in asthma management by modulating key inflammatory and bronchoconstrictive pathways. Stigmasterol exhibits anti-inflammatory and antioxidant effects in murine asthma models by targeting the substance-P receptor (NK1-R), reducing IL-13-induced airway hyper-responsiveness, mucus hypersecretion, and oxidative stress [21]. Gallic acid attenuates allergic inflammation by suppressing IL-33-mediated group 2 innate lymphoid cell (ILC2) activation through inhibition of the MyD88/NF- $\kappa$ B pathway, thereby lowering Th2 cytokines like IL-5 and IL-13 [22]. Kaempferol inhibits mast cell-derived prostaglandin D2 (PGD2) and F2 $\alpha$  (PGF2 $\alpha$ ) by suppressing COX-2 and cytosolic phospholipase A2 (cPLA2) signaling, mitigating airway smooth muscle hypertrophy and bronchoconstriction [23]. Caffeic acid derivatives, such as glycosylated caffeic acid phenylether ester (G-CAPE), inhibit NF- $\kappa$ B activation, reducing neutrophil infiltration and clinical respiratory scores in equine asthma models [24]. Acalyphin from *Acalypha indica* demonstrates anticholinergic and antihistaminic

activity, stabilizing mast cells and reducing leucocytosis in preclinical models [25]. These compounds may contribute to the overall anti-asthmatic effect by modulating multiple pathways involved in bronchoconstriction and inflammation (Figure 3). This study underscores the potential of *Acalypha indica*'s phyto-constituents as multi-target agents for asthma management, addressing gaps in current therapies. By simultaneously targeting PDE4B (to enhance cAMP signaling and reduce inflammation), M3 receptors (to inhibit bronchoconstriction), IL-13 (to suppress Th2 polarization), and ALOX (to limit leukotriene production), these compounds offer a holistic approach to mitigating airway hyper-responsiveness and remodeling. The integration of computational docking with traditional and experimental data provides a robust foundation for further research, including in vitro and in vivo validation of efficacy and safety. Given the plant's historical use and demonstrated preclinical benefits, its phyto-constituents could serve as scaffolds for developing safer, more effective asthma therapeutics, particularly for patients with steroid-resistant or severe phenotypes. Future studies should focus on isolating bioactive compounds, optimizing bioavailability, and evaluating synergistic interactions to harness their full therapeutic potential.

### 3. LIMITATIONS

This study is constrained by its reliance on in-silico methods. Although molecular docking offers important insights into potential interactions, it is essential to conduct experimental validation to substantiate these results. Additional research is required to evaluate the efficacy and safety of *Acalypha indica* Linn and its phytoconstituents using both in-vitro and in-vivo models.



#### 4. CONCLUSION

The computational molecular docking study highlights the anti-asthmatic potential of *Acalypha indica* Linn, demonstrating strong binding affinities of its phyto-constituents such as Stigmasterol, Aurantiamide, Acalyphin, and Kaempferol with key proteins implicated in asthma pathophysiology, including PDE4B, M3 receptor, IL-13, and ALOX. These bioactive compounds exhibit antioxidant, anti-inflammatory, and bronchodilator properties, which collectively contribute to the therapeutic promise of this medicinal plant. The findings suggest that *Acalypha indica* Linn could serve as a natural alternative to conventional asthma treatments by targeting multiple pathways involved in airway inflammation and hyperresponsiveness. This study underscores the need for further experimental validation and clinical trials to establish the efficacy and safety of *Acalypha indica* Linn in asthma management. Integrating its phytoconstituents into therapeutic interventions may enhance treatment outcomes by offering additional benefits such as antioxidant and anti-inflammatory effects. Such advancements could pave the way for safer and more effective management of asthma, addressing limitations associated with current pharmacological approaches.

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#### 7. CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

#### 8. ETHICAL APPROVAL

This study did not involve human participants, animal subjects, or any material that requires ethical approval, as it was conducted entirely through computationally. Therefore, no ethical approval was necessary for this research.

#### 9. ABBREVIATIONS

**PDE4B:** Phosphodiesterase 4B; **M3 receptor:** Muscarinic-3 receptor; **ALOX:** Lipo-oxygenase; **IL-13:** Interleukin 13; **DL:** Drug-likeness; **MW:** Molecular weight; **HBA:** Hydrogen bond Acceptor; **HBD:** Hydrogen bond donor; **MR:** Molar Refractivity; **NoV:** No. of Violation; **OB:** Oral Bioavailability Score; **GIA:** Gastro-intestinal Absorption; **BBB:** Blood Brain Barrier; **HT:** Hepatotoxicity; **CT:** Carcinogenicity; **MT:** Mutagenicity; **LD:** Lethal Dose; **CYP:** Cytochrome P450.

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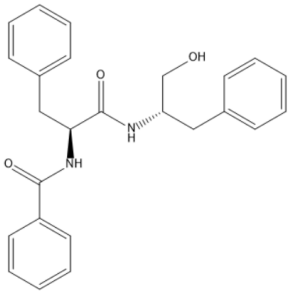
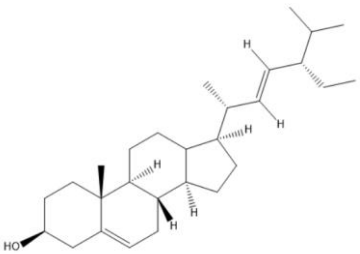


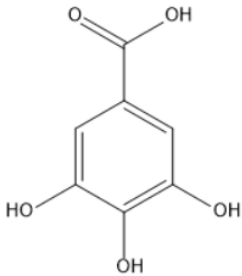
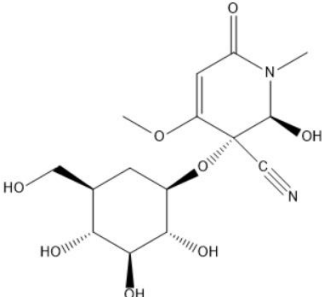
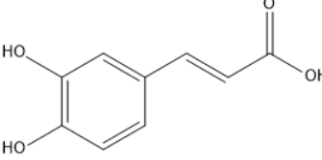
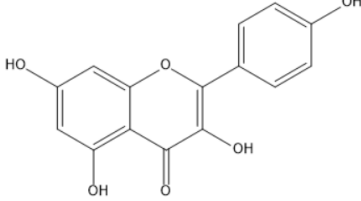
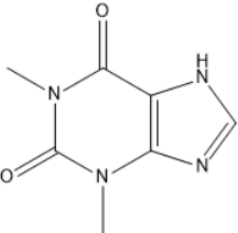
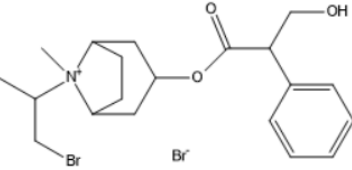
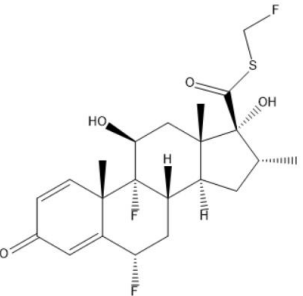
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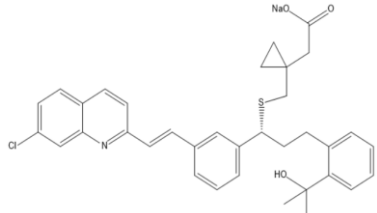
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**Table 1: Structure, Chemical Name, and Formula of Ligands**

Ligands	Structure	Chemical Name	Chemical Formula
Aurantiamide		N-((S)-1-(((S)-1-hydroxy-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl) benzamide	C <sub>25</sub> H <sub>26</sub> N <sub>2</sub> O <sub>3</sub>
Stigmasterol		(3S,8S,9S,10R,14R,17R)-17-((2R,5S,E)-5-ethyl-6-methylhept-3-en-2-yl)-10-methyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol	C <sub>28</sub> H <sub>46</sub> O

Gallic acid		3,4,5-trihydroxybenzoic acid	$C_7H_6O_5$
Acalyphin		(2S,3R)-2-hydroxy-4-methoxy-1-methyl-6-oxo-3-(((1R,2R,3S,4R,5R)-2,3,4-trihydroxy-5-(hydroxymethyl) cyclohexyl) oxy)-1,2,3,6-tetrahydropyridine-3-carbonitrile	$C_{15}H_{22}N_2O_8$
Caffeic acid		(E)-3-(3,4-dihydroxyphenyl) acrylic acid	$C_9H_8O_4$
Kaempferol		3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	$C_{15}H_{10}O_6$
Theophylline		1,3-dimethyl-1H-purine-2,6(3H,7H)-dione	$C_7H_8N_4O_2$
Ipratropium bromide		8-(1-bromopropan-2-yl)-3-((3-hydroxy-2-phenylpropanoyl) oxy)-8-methyl-8-azabicyclo[3.2.1] octan-8-ium bromide	$C_{20}H_{29}Br_2NO_3$
Fluticasone		(6S,8S,9R,10S,11S,13S,14S,16R,17R)-S-(fluoromethyl) 6,9-difluoro-11,17-dihydroxy-10,13,16-trimethyl-3-oxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthrene-17-carbothioate	$C_{22}H_{27}F_3O_4S$

Montelukast		sodium (R,E)-2-(1-(((1-(3-(2-(7-chloroquinolin-2-yl)vinyl)phenyl)-3-(2-(2-hydroxypropan-2-yl)phenyl)propyl)thio)methyl)cyclopropyl)acetate	C <sub>35</sub> H <sub>35</sub> ClN NaO <sub>3</sub> S
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**Table 2: Drug likeness of phytoconstituents of *Acalypha indica* Linn and standard drugs.**

Ligands	Molecular wt	Log p	HBD	HBA	Molar refractivity	No. violation	BS
Aurantiamide	402.5	3.9	3	3	116.61	0	0.55
Stigmasterol	412.7	8.6	1	1	132.7	1	0.55
Gallic acid	170.12	0.7	4	5	39.47	0	0.56
Acalyphin	360.2	-2.9	5	10	80.57	1	0.11
Caffeic acid	180.16	1.2	3	4	47.16	0	0.56
Kaempferol	286.24	1.9	4	6	76.01	0	0.55
Montekulast	570.1	7.7	1	5	167.2	2	0.56
Fluticasone	444.5	3.2	2	8	108.9	0	0.55
Ipratropium bromide	412.4	-2.65	1	4	108.1	0	0.55
Theophylline	180.16	0	1	3	47.14	0	0.55

**Table 3: ADME properties of phytoconstituents of *Acalypha indica* Linn and standard drugs.**

Phytochemicals/ Standard drugs	GIA	BBB	CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4
Aurantiamide	High	Yes	No	Yes	Yes	Yes	Yes
Stigmasterol	Low	No	No	No	Yes	No	No
Gallic acid	High	No	No	No	No	No	No
Acalyphin	Low	No	No	No	No	No	No
Caffeic acid	High	No	No	No	No	No	No
Kaempferol	High	No	Yes	No	No	Yes	Yes
Montekulast	Low	No	No	No	Yes	Yes	Yes
Fluticasone	High	No	No	No	No	No	Yes
Ipratropium bromide	High	No	No	No	No	No	No
Theophylline	High	No	No	No	No	No	No

**Table 4: Toxicity properties of phytochemicals and standard drugs.**

Phytochemicals/ Standard drugs	LD50 Mg/kg	Mutagenicity	Carcinogenicity	Hepatotoxicity
Aurantiamide	550	Inactive	Inactive	Inactive
Stigmasterol	890	Inactive	Inactive	Inactive
Gallic acid	2000	Inactive	Active	Inactive
Acalyphin	3500	Inactive	Inactive	Inactive
Caffeic acid	2980	Inactive	Active	Inactive
Kaempferol	3919	Inactive	Inactive	Inactive
Montekulast	1350	Inactive	Inactive	Inactive
Fluticasone	3000	Inactive	Inactive	Inactive
Ipratropium bromide	380	Inactive	Inactive	Inactive
Theophylline	127	Inactive	Inactive	Inactive

**Table 5 Binding affinity between Phytochemicals and Standard Drugs with their Target Proteins.**

Target Proteins	Phytochemicals & Standard Drug	Binding affinity Kcal/mol	Inhibition constant	Amino acid residues	No. of H-bonds
ALOX5	Acalyphin	-5.38	113.29 uM	ARG A:401, ASP A:170, GLU A:612, PHE A:402, GLN A:15	3
	Aurantiamide	-8.41	680.14 nM	MET A:619, PRO A:668	1
	Caffeic acid	-6.27	25.40 uM	ARG A:401, ASP A:170, LEU A :615, GLU A:614	4
	Gallic acid	-4.64	397.41 uM	SER A:670, ASN A:613, GLU A:614, LEU A:615, ALA A:672	2
	Kaempferol	-5.61	77.27 uM	GLU A:612, SER A:670, ASN A:613, PHE A:402, ALA A:672, GLU A:614, LEU A:615	2
	Stigmasterol	-10.53	19.26 nM	GLU A:615, ARG A:401, ALA A:672, LYS A:83, LEU A:615, TYR A:81, PHE A:402	1
	Montekulast	-9.14	200.87 nM	ASP A:170, ASN A:613, ALA A:672, LEU A:615, PHE A:402, ARG A:401	1
IL13	Acalyphin	-4.20	832.18 uM	ILE C:19, ASN C:22, LEU C:27, LYS C:24, GLN C:23, PRO C:26, ALA C:25	
	Aurantiamide	-6.37	21.56 uM	ALA C:58, LEU C:27	1
	Caffeic acid	-4.52	485.74 uM	ASN C:22, ILE C :19, ALA C:92, PRO C:26, LEU C:27	2
	Gallic acid	-4.87	267.54 uM	ASN C:22, LEU C:27, ILE C:19, PRO C:26	3
	Kaempferol	-4.97	229.10 uM	ASN C:22, ILE C:19, LEU C:27, PRO C:26, ALA C:92	2
	Stigmasterol	-7.47	3.32 uM	ASN C:18, ALA C:58, LYS C:24, ILE C:19, LYS C:24, ALA C:25, PRO C:26	1
	Fluticasone	-5.93	44.72 uM	CYS C:25, CYS C:28, PRO C:26, ASN C:29, LYS C:24, ALA C:58, SER C:57	4
M3 Muscarinic receptor	Acalyphin	-7.09	6.31 uM	ASP A:148, SER A:152, ASN A:153, TYR A:530, CYS A:149, ASN A:508	3
	Aurantiamide	-10.68	14.83 nM	ASN A:153, ASN A:508, PHE A:225	1
	Caffeic acid	-5.44	102.55 uM	ASN A:153, TRP A:200	1
	Gallic acid	-4.04	1.09 mM	ASN A:508, CYS A:533, SER A:152, ASP A:148, TYR A:507	4
	Kaempferol	-6.55	15.93 uM	ASP A:148, SER A:152, ASN A:508, PHE A:225, TRP A:504, TRP A:200, CYS A:149, LEU A:226, ILE A:223, TYR A:507, CYS A:533	3
	Stigmasterol	-4.17	880.49 uM	CYS A:221, LEU A:226, TRP A:526, VAL A:511, ALA A:236, TRP A:504, ILE A:223, TRP A:200, TYR A:507, TYR A:530, LEU A:145	1
	Ipratropium bromide	-8.48	606.02 nM	ASN B:508, VAL A:511, TRP A:200, ALA A:236, ASP A:148	1
PDE4B	Acalyphin	-6.53	16.21 uM	HIS B:278, GLU B:304, ASP B:392, MET B:347, ASP B:346	3
	Aurantiamide	-9.78	68.08 nM	GLU B:304, ASP B:346	1

Caffeic acid	-5.08	189.36 uM	GLU B:304, ASP B:392, MET B:347, ASN B:283, HIS B:234	4
Gallic acid	-4.35	643.45 uM	HIS B:307, THR B:345, ASP B:392, GLU B:304, ASP B:275	4
Kaempferol	-6.53	16.39 uM	GLN B:417, SER B:282, GLU B:509, THR B:511, LEU B:502, LYS B:505, LEU B:510	5
Stigmasterol	-12.00	1.60 nM	ASP B:275, HIS B:238, TYR B:233, ILE B:410, PHE B:506, HIS B:234, MET B:347, PHE B:414, MET B:503, PHE B:446	1
Theophylline	-4.98	224.00 uM	GLN B:443, ILE B:410, TYR B:233, PHE B:414, ILE B:410, PHE B:446, THR B:407	1

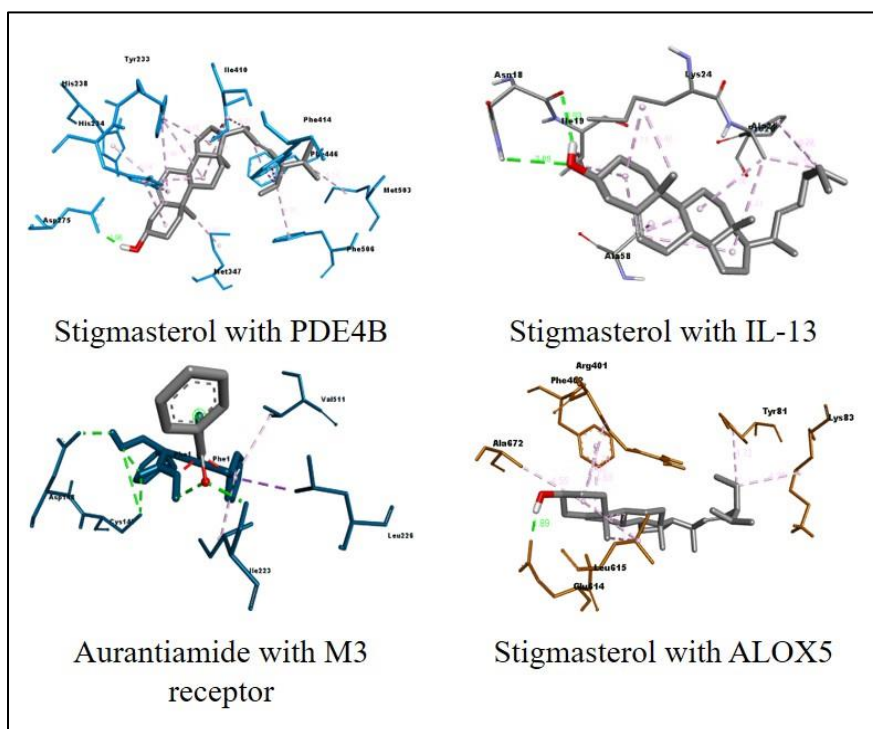


Figure 1: 3D best interactions between phytoconstituents and target proteins

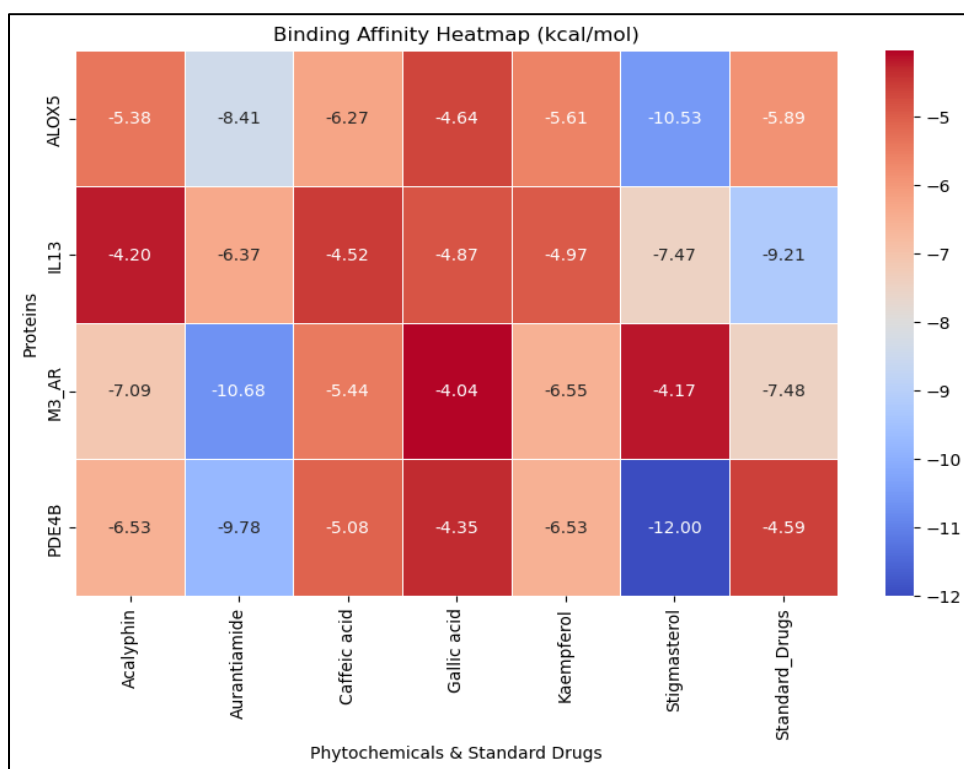


Figure 2: The binding energy between phytochemicals & targets visualized by heatmap.

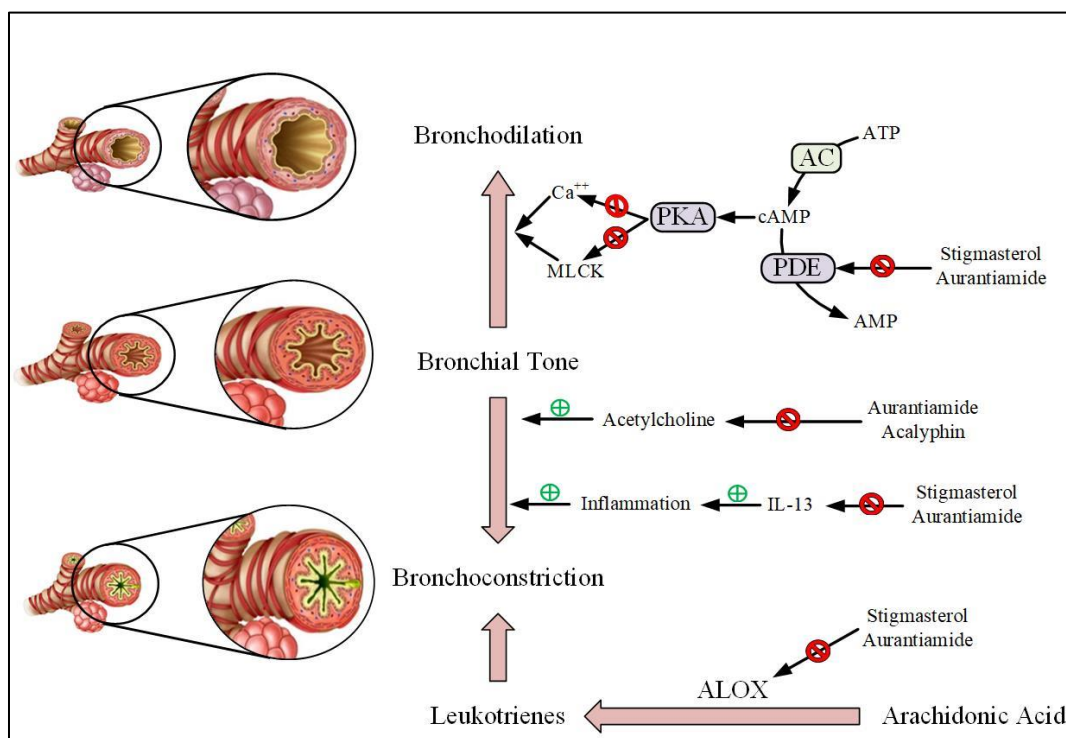


Figure 3: Mode of Action of phytoconstituents for anti-asthmatic activity