Int. J. Pharm. Investigation, 2025; 15(1):10-18.
https://www.jpionline.org

Review Article

Exploring Herbal Antihistaminics-Natural Allergy Fighters for Comprehensive Health Care

Puja Ganeshrao Maldhure, Anita Wanjari*, Kirti Naharwal

Department of Rasashastra and Bhaishajya Kalpana, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, INDIA.

ABSTRACT

Histamine is found in a variety of bodily fluids, platelets, leucocytes, basophils and mast cells in the human body. Mast cells and circulating basophiles store the majority of histamine. Moreover, histamine functions as a neurotransmitter in a variety of cellular physiological processes, including the release of stomach acid, inflammation, allergic reactions and central and peripheral neurotransmission. Histamine is a substance produced by mast cells in the immune system, commonly associated with allergic reactions and their symptoms. Antihistamines are medications designed to counteract the effects of histamine released by the body during allergic responses. Antihistamines block the action of histamine, thereby reducing or alleviating allergy symptoms. The majority of allergic conditions stem from substances such as airborne pollens (from weeds, grass and trees), mites, cockroaches, house dust, animal fur and fungal spores etc., Herbal remedies are increasingly employed to address diverse ailments and enhance various conditions with minimal adverse effects. Antihistaminic effects can be evaluated using extracts from plants or synthetic medications.

Keywords: Histamine, Antihistaminic activity, Mast cells, Basophiles, Allergy.

Correspondence:
Dr. Anita Santoshrao Wanjari
Professor, Department of Rasashastra and Bhaishajya Kalpana, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, INDIA.
Email: anitawanjari7@gmail.com

Received: 07-06-2024;
Revised: 01-07-2024;
Accepted: 27-08-2024.

INTRODUCTION

One of the prevalent illnesses that impact people with a variety of symptoms is allergy. Allergies are a prevalent condition that impacts humans with various symptoms and presentations. In recent years, despite overall improvements in population health, there has been an increase in the occurrence of allergies and asthma.[1] Allergic disorders cause a great deal of morbidity and have a detrimental effect on the economy.[2] Numerous epidemiological investigations have determined the reasons for the rise in upper and lower respiratory tract allergy illness prevalence. Increasing environmental pollution and an increased propensity for people to produce excessive IgE due to a significant shift in the gene pool, altered lifestyles and more knowledge of the illnesses are some of the hypothesized causes.[3] Allergies are increasingly prevalent globally, particularly in developed nations. Currently, around 300 million individuals are impacted by allergies worldwide and projections suggest that an additional 100 million will be affected by 2025.[4] Over the past few decades, extensive study has demonstrated the significance of mast cells, immunoglobulins, lymphocytes and different types of autacoids in the etiopathogenesis of allergy diseases. Despite the abundance of research on the topic, treating allergic illnesses is still far from acceptable. Treatment options for allergic illnesses are severely limited because of their poor efficacy, side effects and difficulties with patient compliance.[5]

The Indian medical system known as *Ayurveda* has recommended a number of medications made from native plant sources to treat allergic diseases including bronchial asthma.[6] Since the ancient period, herbal remedies have been employed for their healing properties, effectively treating numerous ailments. The Indian *Ayurvedic* Medicine system utilizes plants as potent healing components, prompting increased interest in the pharmacological assessment of various plant species employed in traditional medicine systems.[7] *Ayurvedic* texts and other Indian literature document the utilization of various plants to address human health issues. India boasts approximately 45,000 plant species, with numerous believed to possess medicinal properties.[8] In the literature plants used for allergy have shown antiasthmatic, antihistaminic and antiallergic activity. Many phytoconstituents have also proved their effectiveness. In this, we discuss the efficacy of antihistaminic plants and their role in health.

METHODOLOGY

The data was collected from different texts, research articles and e-materials available. The search engines were used to collect the data. PubMed, Science Direct, Scopus, Proquest, Google, Google Scholar and Embase databases were used for collecting the data.

DOI: 10.5530/ijpi.20251739

Histamine and its receptors

Histamine is synthesized and released by several types of human cells, such as mast cells, basophils, lymphocytes, enterochromaffin cells, platelets and histaminergic neurons.[9] Following stimulation, it is stored in vesicles or granules before being released. Histamine exerts its effects on various tissues by interacting with four types of receptors: histamine receptor HR1, HR2, HR3 and HR4, all belonging to the G Protein-Coupled Receptors family (GPCRs).[10] The H1 Receptor (HR1), encoded by a gene on human chromosome 3, is responsible for numerous allergic symptoms like itching, runny nose, bronchial constriction and intestinal smooth muscle contraction. Histamine presence stabilizes the receptor in its active state.

Mast cell stabilizing activity

Mast cells, a type of connective tissue, are closely associated with histamine. The release of histamine by mast cells plays a vital role in the body's inflammatory response.[11] Mast cells, also known as mastocytes, play a crucial role in monitoring the immune system of the human body.[12] These large cells originate from hematopoietic progenitor cells and are found in various tissues, including the oral cavity, conjunctiva, nose and mucosa of the lungs and digestive tract.[13]

Mast cells that have been activated by an antigen start subcellular signalling pathways that release a number of mediators, such as histamine, chymase, hydrogen peroxide, tryptase and cytokines.[14] This leads to the development of allergic reactions. Thus, mast cell stabilizers play a crucial role in preventing various allergic and inflammatory reactions. By stabilizing mast cells, these medications can help reduce the severity and frequency of allergic reactions, making them valuable in the treatment of conditions such as asthma, allergic rhinitis (hay fever) and allergic conjunctivitis.

Many adverse effects, including as anxiety, weariness, headaches, drowsiness and bleeding, are associated with conventional pharmacotherapy's low effectiveness.[15] Thus, the demand for safe and efficient mast cell stabilizers arises. Plants are a great place to look for new drugs. Strong antioxidants, anti-inflammatory agents and histamine release inhibitors are found in plants high in polyphenols.[16]

Antihistamine

The treatment of allergic diseases involves the use of antihistamines.[17] They are helpful in managing allergies brought on by histamine release. Antihistamine medications, then, alleviate allergy symptoms by maintaining the inactive form of the receptor and preventing the effects of histamine.[18] The studies related herbs with antihistaminic activity mentioned in Table 1[19-33] and Phytoconstituents of herbs having antihistaminic activity mentioned in Table 2.[34-82]

DISCUSSION

Ayurveda, an Indian medical system, has prescribed a number of medications made from locally available plant sources to treat allergy diseases and bronchial asthma.[83] Plants have served as medicinal remedies since ancient times, providing treatments for various common ailments throughout human history. Since the dawn of civilization, humans have sought outremedies for different illnesses through their own methods.[84] The assessment of the pharmacological properties of different plants utilized in traditional medicine is gaining more and more attention.

Many human cells, including basophils, mast cells, lymphocytes, histaminergic neurons, platelets and enterochromaffin cells, are responsible for the synthesis and release of histamine.

The inflammatory reaction is set off by histamine. Histamine is produced by basophils and mast cells in the surrounding connective tissues in response to invasive infections. White blood cells and some proteins can more easily enter infected tissues through capillaries that are more permeable due to histamine.

Antihistamines are a type of medicine that is often used to treat a number of allergic disorders. The body's overproduction of histamine causes allergic and inflammatory reactions. Natural remedies have historically been used to counteract the effects of histamine.

Several plants and their derived natural products have been reported as safe, effective and inexpensive antiallergic agents. viz, as per G Sridevi *et al., Ocimum sanctum* demonstrates efficacy in treating asthma by stabilizing mast cells, suppressing IgE and inhibiting inflammatory mediator release, based on experimental findings. According to P. Venkatesh *et al., Curculigo orchioides* rhizomes contain alkaloids, polyphenols, saponins, steroids and tannins, which collectively contribute to its medicinal properties, including allergy alleviation. Dinesh Kumar *et al.* 2011 found that, the bark extract of *Ailanthus excelsa Roxb*. significantly reduced paw volume, potentially by inhibiting antigen-antibody reactions or acting as an antihistamine. It also decreased clonidine-induced catalepsy by possibly antagonizing H1 receptors, indicating significant antihistaminic activity. Similarly, as per Rahul Hazare *et al.*, both the ethanolic extract and essential oil of *Piper betel* Linn. demonstrated antihistaminic properties, inhibiting histamine-induced contractions in guinea pig tracheal and ileum preparations, likely through H1 receptor antagonism. Dnyaneshwar J Taur *et al.*, demonstrated *Clitoria ternatea* L. root extract, known for its anti-inflammatory effects, effectively reduced clonidine-induced catalepsy, suggesting antihistaminic activity mediated via H1 receptor antagonism.

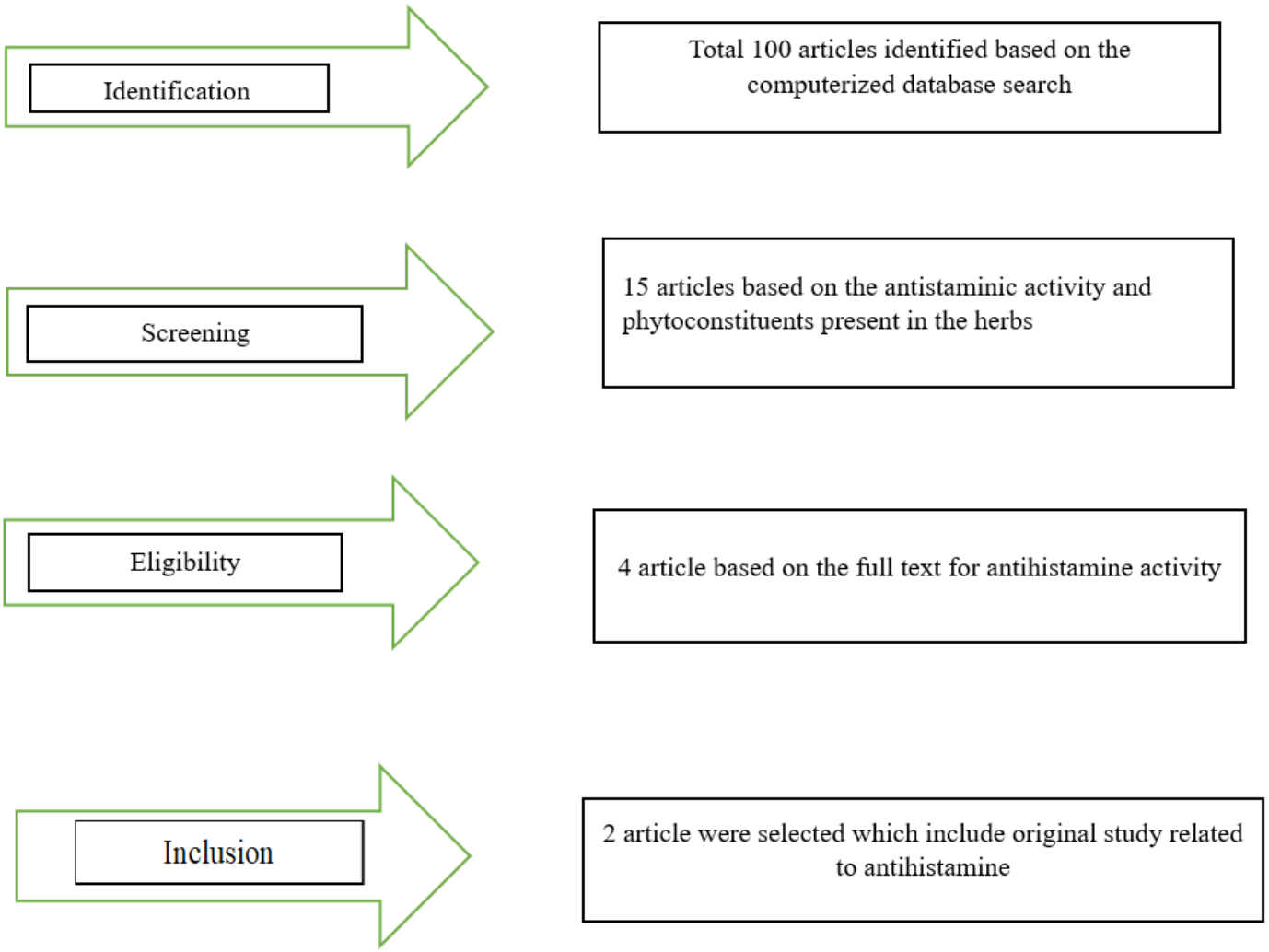
On other hand, according to Dnyaneshwar J *et al.*, Ethanol extract of *Abrus precatorius* Leaves (EAPL) possesses significant antihistaminic activity, as demonstrated by its inhibition of clonidine-induced catalepsy, mediated by histamine through H1

Table 1: The studies related herbs with antihistaminic activity.

Sl. No.	Author and References	Journal and YOP	Study type	Therapeutic regimen	Sample size	Outcome
1.	G Sridevi *et al.*, 2008	The Internet Journal of Pharmacology.	*In vivo*	Alcoholic extract of *Ocimum sanctum.*	Guinea pig (400-600 g).	Research from multiple trials shows that the extract's antihistaminic and antianaphylactic properties are primarily caused by its ability to stabilize mast cells, decrease IgE and prevent the production of inflammatory mediators.[19]
2.	P. Venkatesh *et al.*, 2009	Journal of Ethnopharmacology.	*In vivo*	Alcoholic extract of *Curculigo orchioides* rhizomes.	Male Swiss albino mice (20-25 g).	This result shows that mast cell degranulation and immediate-type allergy reactions arising from mast cells are inhibited by COR.[20]
3.	Dinesh Kumar *et al.* 2011	Pharmacognosy Research.	*In vitro* and *In vivo.*	Aqueous extract of stem barks of *Ailanthus excelsa* Roxb.	Isolated adult goat tracheal tissue albino mice (20-25 g), albino rats (150-200 g).	The aqueous extract of *Ailanthus excelsa* Roxb. stem bark exhibits strong antihistaminic action (H1-antagonist) and is thought to have adaptogenic, bronchodilatory and anti-inflammatory properties.[21]
4.	Rahul Hazare *et al.*, 2011	African Journal of Pharmacy and Pharmacology.	*In vitro* and *In vivo*	Ethanolic extract and essential oil extract of leaves of *Piper betel* Linn.	Isolated guinea pig tracheal chain, Isolated guinea pig ileum, Guinea pigs (350-400 g).	*Piper betel* Linn essential oil and ethanolic extract have antihistaminic properties.[22]
5.	Dnyaneshwar J Taur *et al.*, 2011	Journal of Basic and Clinical Pharmacy.	*In vivo*	Ethanol extract of *Clitoria ternatea* L. root.	Swiss albino mice (25-30 g).	The study found that medications with antihistaminic potential reduce catalepsy produced by clonidine, indicating that the ethanol extract of the roots of *Clitoria ternatea* has antihistaminic properties.[23]
6.	Dnyaneshwar J *et al.*, 2011	Oriental Pharmacy and Experimental Medicine.	*In vivo*	Ethanol extract of *Abrus precatorius* leaves.	Swiss albino mice (25-30 g).	EAPL has antihistaminic activity since medications with antihistaminic potential prevent clonidine-induced catalepsy.[24]

Sl. No.	Author and References	Journal and YOP	Study type	Therapeutic regimen	Sample size	Outcome
7.	Dnyaneshwar J Taur *et al.*, 2011	Chinese Journal of Natural Medicines.	*In vivo*	Ethanol extract *Coccinia grandis* fruit.	Wistar rats (150-170 g) Swiss albino Mice (25-30 g).	ECGF helps stabilize mast cell degranulation triggered by antigens and prevents the release of histamine during an anaphylactic reaction.[25]
8.	Yoke Keong Yong *et al.*, 2013	BMC Complementary and Alternative Medicine.	*In vivo*	Aqueous extract of *Bixa orellana.*	Sprague-Dawley rats weighing (200-250 g).	Its anti-inflammatory properties could be attributed to the active component of the aqueous extract. It remains to be determined if it functions via stabilizing mast cells.[26]
9.	Pandy Vijayapandi *et al.*, 2013	African Journal of Traditional, Complementary and Alternative Medicines.	*In vitro*	Aqueous, acetone, hexane and methanol extracts of *Acorus calamus* leaves.	Isolated guinea pig ileum.	*Acorus calamus* leaves extracts exerts antihistaminic effect in guinea pig ileum.[27]
10.	Sunita Thakur *et al.* 2013	International Journal of Pharmaceutical Research and Allied Sciences.	*In vivo*	Ethanolic seed extract of *Moringa oleifera.*	Wistar albino rats (150-170 g)	*Moringa oleifera* ethanolic extract has the ability to stabilize mast cells and has anti-allergic properties, making it useful in the treatment of asthma.[28]
11.	Sangilimuthu Alagar Yadav *et al.*, 2015	Journal of Complementary and Integrative Medicine.	*In vivo* and *in vitro*.	Methanol extract of *Tragia involucrata* L.	Isolated guinea pig ileum, Guinea pigs (250-350 g)	On histamine-induced guinea pigs, isolated 5-hydroxy-1-methylpiperidin-2-one from *Tragia involucrata* L. has strong antihistamine properties.[29]
12.	Hassan M Qureshi *et al.*, 2015	Pakistan Veterinary Journal.	*In vitro*	Ethanolic and aqueous extract of *Murraya koenigii* leaves.	Isolated tissues of guinea pig ileum, rabbit trachea and jejunum.	*Murraya koenigii* leaf extracts, both aqueous and ethanolic, have potential applications in the treatment of gastrointestinal and respiratory conditions.[30]
13.	Firdous A. *et al.*, 2017	Annals of plant sciences.	*In vivo*	Ethnolic extract of *cuscuta reflexa* Roxb.	Male albino rats (150-200 g).	The study shows that the ethnolic extract of *Cuscuta reflexa* stabilizes mast cells in experimental animals.[31]
14.	Ms. Asha Jadhav *et al.*, 2018	Int. Journal of Pharmaceutical Sciences and Medicine (IJPSM).	*In vitro*	Methanol extract of *Raphanus sativus* L.	Goat tracheal tissue.	*Raphanus sativus* L. leaf methanolic extract inhibit variety of contractile stimuli, including histamine.[32]

Sl. No.	Author and References	Journal and YOP	Study type	Therapeutic regimen	Sample size	Outcome
15.	Vandana Athiya *et al,* 2019	Journal of Drug Delivery and Therapeutics.	*In vivo*	Methanol extract of *Adhatoda vasica.*	Swiss albino mice (25-30 g).	The methanol extract of *Adhatoda vasica* leaves has antihistaminic activity since medications with antihistaminic potential reduce clonidine-induced catalepsy.[33]



receptors, thereby suggesting its potential as an antihistaminic or mast cell stabilizing agent.

As per Dnyaneshwar J Taur *et al.*, the ethanol extract of *Coccinia grandis* fruit contains saponin, steroids, alkaloids, flavonoids and glycosides. Saponins stabilize mast cells, exhibiting antiallergic and antihistaminic properties. Glycosides have antiasthmatic effects by relaxing tracheal smooth muscle and reducing allergies. Flavonoids like apigenin and luteolin possess bronchodilator activity, inhibiting histamine release for antiallergic effects. ECGF stabilizes mast cells, inhibits histamine release and prevents catalepsy, showing promise for asthma treatment due to its antiallergic and mast cell stabilizing effects. Yoke Keong Yong *et al.*, found that *Bixa Orellana's* aqueous extract possesses anti-inflammatory properties by reducing vascular permeability through the suppression of biochemical mediators such as VEGF and NO in tissues, indicating its potential as an anti-inflammatory agent. As per Pandy Vijayapandi *et al., Acorus calamus* contains a diverse range of phytochemicals, including terpenoids, steroids, xanthones, lignans, flavones, glycosides, flavonoids, saponins,

Table 2: Phytoconstituents of herbs having antihistaminic activity.

Sl. No.	Name of herbs	Phytoconstituents
1.	*Ailanthus excelsa* Roxb.	Quassinoids - Stem bark contains quassinoids like 1,4-dihydroexcelsin, excelsin,[34,35] 3, 4, dihydroexcelsin, 2, 4-dihydroexcelsin,[36] glaucarubol,13,18-dehydroexcelsin,[37] ailanthinone, ailanex A, ailanex B, polyandrol and glaucarubolon,[38-39] glaucarubol,[40] Triacontane and hexatriacontane.[41]
2.	*Piper betel* Linn.	Phytochemical constituents of the essential oil of the betel leaf are terpenes and phenols,[42] Hydroxychavicol (HC)/Hydroxychavicol Acetate (HCA), Chavibetol,[43] Piperbetol, allylpyrocatechol, carvacol, PiperitolCaryophyllene, Piperbetol, Eugenol, Isoeugenol, Safrole, Chavicol, Anethole,[44] β-sitosterol, Chavibetol,cadinene,[45] Hydroxychavicol.[46]
3.	*Clitorea ternatea* L.	1,1-diphenyl-2-picrylhydrazyl,[47] β carotene, taraxerol and teraxerone, Stigmast-4-ene-3,6, diene,starch,resins and tannins.[48]
4.	*Cuscuta reflexa* Roxb.	Cuscutarosides A and B, steroidal glucoside, 2H-pyran-2-one glucosides, 7β-methoxy-βsitosterol 3-O-β-glucopyranoside.[49]
5.	*Curculigo orchioides*	n-hexadec-9,11-dienyl cinnamate, n-heneitriacont-13-en-5,10-diol hex-2'-en-1'- oate, n-decan-3-olyl pent-3'en-1'-oate, n-tridecanyl-hex-2',4'- dien-1'-oate.[50]
6.	*Tragia Involucrata* L.	T. involucrata leaf; contains, vinyl hexylether and 2-methylnonane,[51] Antihistamine 5-hydroxy-1-methylpiperidin-2-one.
7.	*Bixa orellana* L.	Pentanoic acid, Phenol, 2-Butamine, Acetic acid, Benzoic acid. Pantolactone,[52] Bixein, Isobixin, Croceti, Bixaghanene, Ellagic acid, Tryptophan, Tomenstosic acid, Salicylic acid, Falvonoid, Phenylalanine, Threonine, Bisulfates, Sterols, Saponins, Tannis,[53] Terpenoids, Carotenoids.[54]
8.	*Acorus calamus* Linn.	Glycosides, flavonoids, saponins, tannins, polyphenolic compounds, mucilage, volatile oil,[55] Cisisoelemicine, cis and trans isoeugenol and their methyl ethers, P-cymene, α-selinene, camphene, bgurjunene, β-cadinene, camphor, terpinen-4-ol, βasarone, αasarone, elemicine.[56]
9.	*Abrus precatorius* Linn.	Abrin, trigonelline,[57] hemiphloin, abruslactone A,[58] abrusoside A,[59] abrusoside B, abrusoside C, abrusoside D,[60] Xylosegalactose, arabinose,[61] hypaphorine, precatorine,[62] glycyrrhizin,[63] montanyl alcohol, pinitol, inositol D monomethyl ether.[64]
10.	*Coccinia grandis* Linn.	2-methoxy-4-vinylphenol, 12-octadecadienoic acid, benzofuranone, 13-octadecadienol 9, phenol-2-methoxy-5(1-propenyl), Phenol, 3,7,11,15-tetramethyl-2- hexadecen-1-ol, 2.4-bis(1,1-dimethylethyl), undecanol, 2(3h)-furanone, 2-methyl-z,z-3, hexadecanoic acid methyl ester, β-sitosterol acetate, campoesterol, stigmatosterol, tocopherol, campesterol and ethisteron.[65]
11.	*Murraya koenigii* Linn.	Mahanine, Mahanimbine, Murrayanol,[66-68] O-Methylmurrayamine A, Koenigicine, Murrayone (Coumarine), Mahanimbicine, Bicyclomahanimbicine, Phebalosin,[69-70] Euchrestine B, Girinimbilol, Isolongifolene
12.	*Oscimum sanctum*	ß-caryophyllene, methyl eugenol,[71,72] (E)-caryophyllene, Eugenol and β-elemene,[73] methyl chavicol and linalool,[74] β-bisabolene, 1,8-cineole,[75] Isocaryophyllene.
13.	*Raphanus Sativus* L	Concentration of calcium, potassium, sodium, fiber, macronutrients, fatty acids and nonflavonoid polyphenols is high in leaves.Flavonoids- anthocyanins, flavanol catechinTerpenes and derivatives-β-carotene and phytol.[76]
14.	*Adathoda vasica* Nees.	Quinazoline alkaloid, vasicine (1, 2, 3, 9-tetrahydropyrrole [2, 1-b] quinozolin-3-ol,[77] $C_{11}H_{12}N_2O$), adhatonine, adhavasinone, adhatodine, vasicinol, vasicinone, vasicinolone, N-oxide vasicine, vasicol, Betaine, steroid β-sitosterol and alkanes.[78]
15.	*Moringa oleifera*	Seeds contain high concentrations of benzylglucosinolate, 4-(α-1-rhamnopyranosyloxy)-benzylglucosinolate, 4-(α-l-rhamnosyloxy) benzylisothiocyanate, O-ethyl-4-(α-l-rhamnosyloxy) benzyl carbamate.[79-82]

tannins, polyphenolic compounds, mucilage, glucoside, alkaloids and essential oils like calamen, clamenol, calameon, asarone and sesquiterpenes. Both methanol and aqueous extracts of its leaves exhibit antimuscarinic activity, suggesting possible bronchodilator effects and validating its traditional use in asthma treatment. According to, Sunita Thakur *et al., Moringa oleifera* extract contains steroids, saponins, alkaloids, flavonoids and glycosides. Glycoside, saponins stabilize mast cells, while flavonoids like apigenin and luteolin inhibit histamine release from basophils and neutrophils. They also suppress histamine release triggered by 48/80, showing promise for asthma treatment due to anti-allergic and mast cell stabilizing effects. Sangilimuthu Alagar Yadav *et al.*, identified 5-hydroxy-1-methylpiperidin-2-one isolated from *Tragia involucrata* L. leaves acts as a potent muscle relaxant, bronchodilator and anti-allergic agent, particularly effective against histamine-induced muscle contraction in guinea pigs. It exhibits strong antihistamine properties as evidenced by its high docking score, energy and interactions.

According to Hassan M Qureshi *et al.*, both ethanolic and aqueous extracts of *Murraya koenigii* Linn. demonstrated antihistaminic and anticholinergic activities. They caused a rightward shift in histamine concentration response curves and dose-dependent relaxation of pre-contracted isolated rabbit trachea and jejunum tissue, indicating potential for treating airway and gastrointestinal disorders. Firdous A. *et al.*, found that, the ethanolic extract of *Cuscuta reflexa* demonstrated mast cell stabilizing activity, likely due to its flavonoids and saponins. As per Ms. Asha Jadhav *et al.*, The methanolic extract from *Raphanus sativus* L. leaves contains saponins, flavonoids, tannins, glycosides and carbohydrates. It significantly inhibits dose-dependent contraction induced by histamine, suggesting competitive antagonism for H1 receptors on smooth muscle. This indicates its ability to effectively inhibit responses to various contractile stimuli, including histamine, thus possessing antihistaminic action. According to Vandana Athiya *et al., Adathoda vasica* extract contains carbohydrates, glycosides, alkaloids, saponins, flavonoids, tannins and phenolic compounds. Its methanol extract shows significant antihistaminic activity, likely due to its H1-antagonist properties, contributing to bronchodilating, anti-inflammatory and adaptogenic effects.

ACKNOWLEDGEMENT

The authors acknowledge the support given by DMIHER university, VC, DMIHER(DU).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HR: Histamine receptor; **GPCR:** G protein-coupled receptors; **EAPL:** Ethanol extract of *Abrus precatorius* leaves; **ECGF:** Ethanol extract *Coccinia grandis* Fruit; **HCA:** Hydroxychavicol acetate; **IgE:** Immunoglobulin E.

REFERENCES

1. Ring J, Krämer U, Schäfer T, Behrendt H. Why are allergies increasing? Curr Opin Immunol. 2001;13(6):701-8. doi: 10.1016/S0952-7915(01)00282-5.
2. Spector SL. Overview of comorbid associations of allergic rhinitis. J Allergy Clin Immunol. 1997; 99(2):S773-80. doi: 10.1016/s0091-6749(97)70126-x, PMID 9042070.
3. Hansen I, Klimek L, Mösges R, Hörmann K. Mediators of inflammation in the early and the late phase of allergic rhinitis. Curr Opin Allergy Clin Immunol. 2004;4(3):159-63. doi: 10.1097/00130832-200406000-00004, PMID 15126935.
4. Salib RJ, Drake-Lee A, Howarth PH. Allergic rhinitis: past, present and the future. Clin Otolaryngol Allied Sci. 2003;28(4):291-303. doi: 10.1046/j.1365-2273.2003.00706.x, PMID 12871241.
5. Bouabdallah S, Sobhy HA, Adetuyi BO, Eldahshan OA, Egbuna C. Important antihistaminic plants and their potential role in health. Phytochem Drug Discov Cent Nerv Syst Disord Biochem Ther Eff. 2023:385-96.
6. Mitra S, Gopumadhavan S, Rafiq M, Venkataranganna M. Antihistaminic and antianaphylactic activity of HK-07, a herbal formulation. Indian J Pharmacol. 2005;37(5):300-3. doi: 10.4103/0253-7613.16853.
7. Kumar D, Bhat ZA, Singh P, Bhujbal SS, Deoda RS. Antihistaminic activity of aqueous extract of stem bark of *Ailanthus excelsa* Roxb. Pharmacogn Res. 2011;3(3):220-4. doi: 10.4103/0974-8490.85014, PMID 22022173.
8. Taur DJ, Patil RY. Some medicinal plants with antiasthmatic potential: a current status. Asian Pac J Trop Biomed. 2011;1(5):413-8. doi: 10.1016/S2221-1691(11) 60091-9, PMID 23569804.
9. Huang H, Li Y, Liang J, Finkelman FD. Molecular regulation of histamine synthesis. Front Immunol. 2018;9:1392. doi: 10.3389/fimmu.2018.01392, PMID 29973935.
10. Nema S, Shrivastava S. Allergy and antihistamine: the significance of medicinal plants and their relevance in drug repurposing. ISBN: Book DOI: Price. 2021;747:21.
11. Amin K. The role of mast cells in allergic inflammation. Respir Med. 2012;106(1):9-14. doi: 10.1016/j.rmed.2011.09.007, PMID 22112783.
12. Zhao W, Gan X, Su G, Wanling G, Li S, Hei Z, *et al.* The interaction between oxidative stress and mast cell activation plays a role in acute lung injuries induced by intestinal ischemia-reperfusion. J Surg Res. 2014;187(2):542-52. doi: 10.1016/j.jss.2013.10.033 , PMID 24275574.
13. Berridge MJ. Cell stress, inflammatory responses and cell death. Cell Signal Biol. 2012;11:11.1-11.28.
14. Oh B, Lee CH. Nanofiber-coated drug eluting stent for the stabilization of mast cells. Pharm Res. 2014;31(9):2463-78. doi: 10.1007/s11095-014-1341-3, PMID 24664448.
15. Amit A, Saxena VS, Pratibha N, Bagchi M, Bagchi D, Stohs SJ. Safety of a novel botanical extract formula for ameliorating allergic rhinitis. Toxicol Mech Methods. 2003;13(4):253-61. doi: 10.1080/713857188, PMID 20021150.
16. Obrenovich ME, Nair NG, Beyaz A, Aliev G, Reddy VP. The role of polyphenolic antioxidants in health, disease and aging. Rejuvenation Res. 2010;13(6):631-43. doi: 1 0.1089/rej.2010.1043, PMID 20818981.
17. Simons FE, Simons KJ. H1 antihistamines: current status and future directions. World Allergy Organ J. 2008;1(9):145-55. doi: 10.1186/1939-4551-1-9-145, PMID 23282578.
18. Stojković N, Cekić S, Ristov M, Ristić M, Đukić D, Binić M, *et al.* Histamine and antihistamines/Histamin i antihistamini. Acta Fac Med Naissensis. 2015;32(1):7-22. doi: 10.1515/afmnai-2015-0001.
19. Sridevi G, Gopkumar P, Ashok S, Shastry C. Pharmacological basis for antianaphylactic, antihistaminic and mast cell stabilization activity of *Ocimum sanctum*. Internet J Pharmacol. 2008;7(1).
20. Venkatesh P, Mukherjee PK, Kumar SN, Nema NK, Bandyopadhyay A, Fukui H, *et al.* Mast cell stabilization and antihistaminic potentials of *Curculigo orchioides* rhizomes. J Ethnopharmacol. 2009;126(3):434-6. doi: 10.1016/j.jep.2009.09.019, PMID 19781614.
21. Kumar D, Bhat ZA, Singh P, Bhujbal SS, Deoda RS. Antihistaminic activity of aqueous extract of stem bark of *Ailanthus excelsa* Roxb. Pharmacogn Res. 2011;3(3):220-4. doi: 10.4103/0974-8490.85014, PMID 22022173.
22. Hajare R, Darvhekar VM, Shewale A, Patil V. Evaluation of antihistaminic activity of *Piper betel* leaf in guinea pig. Afr J Pharm Pharmacol. 2011;5(2):113-7.
23. Taur DJ, Patil RY. Antihistaminic activity of *Clitoria ternatea* L. roots. J Basic Clin Pharm. 2010;2(1):41-4. PMID 24826001.
24. Taur DJ, Patil RY. Antihistaminic activity of Abrus precatorius using clonidine induced catalepsy in mice. Orient Pharm Exp Med. 2012;12(1):11-4. doi: 10.1007/s13596-011 -0046-y.

25. Taur DJ, Patil RY. Mast cell stabilizing, antianaphylactic and antihistaminic activity of *Coccinia grandis* fruits in asthma. Chin J Nat Med. 2011;9(5):359-62.
26. Yong YK, Zakaria ZA, Kadir AA, Somchit MN, Lian EC. G, Ahmad Z. Chemical constituents and antihistamine activity of *Bixa orellana* leaf extract. BMC Complement Altern Med. 2013;13:1-7.
27. Vijayapandia P, Annabathina V, SivaNagaSrikanth B, Manjunath V, Boggavarapu P, Rajendra Prasad K, et al. *In vitro* anticholinergic and antihistaminic activities of *Acorus calamus* Linn. leaves extracts. Afr J Trad Complement Altern Med. 2013;10(1):95-101.
28. Thakur S, Verma A. Antihistaminic effect of *Moringa oleifera* seed extract. Int J Pharm Res Allied Sci. 2013;2:56-9.
29. Alagar Yadav S, Ramalingam S, Jabamalai Raj A, Subban R. Antihistamine from *Tragia involucrata* L. leaves. J Complement Integr Med. 2015;12(3):217-26. doi: 10.1515/jcim-2015-0015, PMID 26043438.
30. Qureshi HM, Omer MO, Ashraf M, Bukhsh A, Chaudhry MA, Imran MS. Evaluation of antihistaminic and anticholinergic activities of *Murraya koenigii* Linn.
31. Mala FA, Sofi MA. Evaluation of antihistaminic Activity of herbal drug isolated from *Cuscuta reflexa* Roxb. Ann Plant Sci. 2017;6(11):1807-10. doi: 10.21746/aps.2017.6.11.15.
32. Ms. Jadhav A. Ms. Nilam Jadhav Adarsh College of Pharmacy, Kundal Road, Bhawani Nagar, Vita-415. Vol. 311.
33. Athiya V, Gupta S, Chourasiya A. Phytochemical screening and assessment of *Adhatoda vasica* (leaf) for antihistaminic activity. J Drug Deliv Ther. 2019;9(4-s):1092-5.
34. Tripathi AK, Jain DC. Excelsin an insect feeding deterrent isolated from *Ailanthus excelsa* (Simaroubaceae). J Phytol Res. 1993;7(4):323-5. doi: 10.1002/ptr.2650070414.
35. Khan SA, Zuberi SS, Shamsuddin KM. Isolation and structure of Excelsin, a new quassinoid from *Ailanthus excelsa*. Indian J Chem:198019B: 183-4.
36. Bhatia N, Sahai M, Khosa RL. Chemical studies on *Ailanthus excelsa*. J Indian Chem Soc. 1985;62:75.
37. Khan SA, Shamsuddin KM. Quassinoids from *Ailanthus excelsa*. Indian J Chem. 1978;16B: 1045.
38. Joshi B, Sharma RP, Khare A. New quassinoids from *Ailanthus excelsa*. Pandey. Med Chem Res. 2004; 13(8/9):781-9.
39. Joshi BC, Pandey A, Sharma RP, Khare A. Quassinoids from *Ailanthus excelsa*. Phytochemistry. 2003;62(4):579-84. doi: 10.1016/s0031-9422(02)00493-4, PMID 12560029.
40. Khan SA, Shamsuddin KM. Isolation and structure of 13, 18-dehydroexcelsin, a quassinoid and glaucarubol from *Ailanthus excelsa*. Phytochemistry. 1980;19(11):2484-5. doi: 10.1016/S0031-9422(00)91062-8.
41. Mehta CR, Patel CN. Chemical examination of the bark of *Ailanthus excelsa*, Roxb. Part I. Indian J Pharmacol. 1959;21:143-5.
42. Atal CK, Dhar KL, Singh J. The chemistry of Indian Piper species. Lloydia. 1975;38(3):256-64. PMID 1095880.
43. Rathee JS, Patro BS, Mula S, Gamre S, Chattopadhyay S. Antioxidant activity of *Piper betel* leaf extract and its constituents. J Agric Food Chem. 2006;54(24):9046-54. doi: 10.1021/jf061679e, PMID 17117789.
44. Zeng HW, Jiang YY, Cai DG, Bian J, Long K, Chen ZL, *et al.* methylpiperbetol, piperol A and piperol B: a new series of highly specific PAF receptor antagonists from Piper betel. Planta Med. 1997;63:296-8.
45. Samy J, Sugumaran M, Lee KL. Herbs of Malaysia. Malaysia: Federal Publications Sdn Berhad; 2005. p. 187.
46. A Modern Herbal/ Betel-Herb Profile and Informationhttp: [cited Oct 1 2007]. Available from: http://www.botanical.com/html.
47. Braca A, Sortino C, Politi M, Morelli I, Mendez J. Antioxidant activity of flavonoids from *Licania linaniaeflora*. J Ethnopharmacol. 2002;79(3):379-81. doi: 10.1016/s0378-8741(01)00413-5, PMID 11849846.
48. Tiwari RD, Gupta RK. Chemical examination of the leaves of *Clitoria ternatea*. J Indian Chem Soc. 1959;36:243-6.
49. Aung TT, Xia MY, Hein PP, Tang R, Zhang DD, Yang J, *et al.* Chemical constituents from the whole plant of *Cuscuta reflexa*. Nat Prod Bioprospect. 2020;10(5):337-44. doi: 10.1007/s13659-020-00265-x, PMID 32954471.
50. Lakshmi N, Kumari S, Sharma Y, Sharma N. New phytoconstituents from the rhizomes of *Curculigo orchioides*. Pharm Biol. 2004;42(2):131-4. doi: 10.1080/13880200490510964.
51. Gobalakrishnan R, Kulandaivelu M, Bhuvaneswari R, Kandavel D, Kannan L. Screening of wild plant species for antibacterial activity and phytochemical analysis of *Tragia involucrata* L. J Pharm Anal. 2013;3(6):460-5. doi: 10.1016/j.jpha.2013.07.001, PMID 29403856.
52. Yong YK, Zakaria ZA, Kadir AA, Somchit MN, Lian EC. Chemical constituents and antihistamine activity of *Bixa orellana* leaf extract. BMC Complement Altern Med. 2013;13(1):1-7.
53. Raddatz-Mota D, Pérez-Flores LJ, Carrari F, Mendoza-Espinoza JA, De León-Sánchez FD, Pinzón-López LL, *et al.* Achiote (*Bixa orellana* L.): a natural source of pigment and vitamin E [*Bixa orellana* L]. J Food Sci Technol. 2017;54(6):1729-41. doi: 10.1007/s13197-017-2579-7, PMID 28559632.
54. Pacheco SD, Gasparin AT, Jesus CH, Sotomaior BB, Ventura AC, Redivo DD, *et al.* Antinociceptive and anti-inflammatory effects of Bixin, a carotenoid extracted from the seeds of *Bixa orellana*. Planta Med. 2019;85(16):1216-24. doi: 10.1055/a-1008-1238, PMID 31546267.
55. Imam H, Riaz Z, Azhar M, Sofi G, Hussain A. Sweet flag. Overview Int J Green Pharm. 2013; 106(67, 65):148.
56. Chandra D, Prasad K. Phytochemicals of *Acorus calamus* (sweet flag). J Med Plants Stud. 2017;5(5):277-81.
57. Ibrahim N. Phytochemical studies of *Abrus precatorius* alkaloids. Herba Hung. 1980;19(3):21-6.
58. Ragasa CY, Lorena GS, Mandia EH, Raga DD, Shen CC. Chemical constituents of *Abrus precatorius*. Am J Essent Oils Nat. Prod. 2013;1(2):7-10.
59. Choi YH, Hussain RA, Pezzuto JM, Kinghorn AD, Morton JF, Abrososides AD. Abrusosides A-D, four novel sweet-tasting triterpene glycosides from the leaves of *Abrus precatorius*. J Nat Prod. 1989;52(5):1118-27. doi: 10.1021/np50065a032, PMID 2691636.
60. Choi YH, Kinghorn AD, Shi XB, Zhang H, Teo BK. Abrusoside A: a new type of highly sweet triterpene glycoside. J Chem Soc Chem Commun. 1989;(13):887-8. doi: 10.1039/c39890000887.
61. Karawya MS, El Gengaihi S, Wassel G, Ibrahim NA. Carbohydrates of *Abrus precatorius*. Fitoterapia. 1981;52:179-81.
62. Ghosal S, Dutta SK. Alakloids of *Abrus precatorius*. Phytochemistry. 1971;10(1):195-8. doi: 10.1016/S0031-9422(00)90270-X.
63. Akinloye BA, Adalumo LA. *Abrus precatorius* leaves-a source of glycyrrhizin. Niger J Pharm. 1981;12:405.
64. Ali E, Malek A. Chemical investigations on *Abrus precatorius* Linn. Beng Kunch. Sci Res Ill. 1966;3:141-5.
65. Putra IM, Fakhrudin N, Nurrochmad A, Wahyuono S. Antidiabetic activity of *Coccinia grandis* (L.) Voigt: bioactive constituents, mechanisms of action and synergistic effects. J Appl Pharm Sci. 2021 December 27;12(1):041-54.
66. Ramsewak RS, Nair MG, Strasburg GM, DeWitt DL, Nitiss JL. Biologically active carbazole alkaloids from *Murraya koenigii*. J Agric Food Chem. 1999;47(2):444-7. doi: 10.1021/jf9805808, PMID 10563914.
67. Joshi BS, Kamat VN, Gawad DH. On the structures of girinimbine, mahanimbine, isomahanimbine, koenimbidine and murrayacine. Tetrahedron. 1970;26(6):1475-82. doi: 10.1016/s0040-4020(01)92976-x, PMID 5419188.
68. Gahlawat DK, Jakhar S, Dahiya P. *Murraya koenigii* (L.) Spreng: an ethnobotanical, phytochemical and pharmacological review. J Pharmacogn Phytochem. 2014;3:109-19.
69. Igara C, Omoboyowa D, Ahuchaogu A, Orji N, Ndukwe M. Phytochemical and nutritional profile of *Murraya koenigii* (Linn.) Spreng leaf. J Pharmacogn Phytochem. 2016;5:7-9.
70. Samanta SK, Kandimalla R, Gogoi B, Dutta KN, Choudhury P, Deb PK, *et al.* Phytochemical portfolio and anticancer activity of *Murraya koenigii* and its primary active.
71. Bhattacharya AK, Kaul PN, Rajeswara Rao BR. Essential oils of *Ocimum gratissimum* L. and Ocimum tenuiflorum L. 1996;40:73-5 (Syn. *Ocimum sanctum* L.) grown in Andhra Pradesh. Indian Perfumer.
72. Kothari SK, Bhattacharya AK, Ramesh S, Garg SN, Khanuja SP. Volatile constituents in oil from different plant parts of methyl eugenol-rich *Ocimum tenuiflorum* L. f. J Essent Oil Res. 2005;17(6):656-8. doi: 10.1080/10412905.2005.9699025. (Syn. O. sanctum L.).
73. Awasthi PK, Dixit SC. Chemical compositions of *Ocimum sanctum* Shyama and *Ocimum sanctum* Rama oils from the plains of Northern India. J Essent Oil Bear Plants. 2007;10(4):292-6. doi: 10.1080/0972060X.2007.10643557.
74. Khan A, Ahmad A, Akhtar F, Yousuf S, Xess I, Khan LA, et al. *Ocimum sanctum* essential oil and its active principles exert their antifungal activity by disrupting ergosterol biosynthesis and membrane integrity. Res Microbiol. 2010;161(10):816-23. doi: 10.1016/j.resmic.2010.09.008, PMID 20868749.
75. Kicel A, Kurowska A, Kalemba D. Composition of the essential oil of *Ocimum sanctum* L. grown in Poland during vegetation. J Essent Oil Res. 2005;17(2):217-9. doi: 10.1080/10412905.2005.9698880.
76. Gamba M, Asllanaj E, Raguindin PF, Glisic M, Franco OH, Minder B, *et al.* Nutritional and phytochemical characterization of radish (*Raphanus sativus*): A systematic review. Trends Food Sci Technol. 2021;113:205-18. doi: 10.1016/j.tifs.2021.04.045.
77. Chowdhury BK, Bhattacharyya P. Adhavasinone: A new quinazolone alkaloid from *Adhatoda vasica* Nees. Chim Ind, (London). 1987;1:35-6.
78. Jain MP, Koul SK, Dhar KL, Atal CK. Novel nor-harmal alkaloid from *Adhatoda vasica*. Phytochemistry. 1980;19(8):1880-2. doi: 10.1016/S0031-9422(00)83845-5.
79. Dahot MU, Memon AR. Nutritive significance of oil extracted from *Moringa oleifera* seeds. J Pharm Univ Karachi. 1985;3:75-80.
80. Anwar F, Bhanger MI. Analytical characterization of *Moringa oleifera* seed oil grown in temperate regions of Pakistan. J Agric Food Chem. 2003;51(22):6558-63. doi: 10.1021/jf0209894, PMID 14558778.

81. Dayrit IM, Alcantar AD, Villasenor IM. Studies on *Moringa oleifera* seeds, Part I. The antibiotic compound and its deactivation in aqueous solution. Philip J Sci. 1990;119:23-32.
82. Guevara AP, Vargas C, Sakurai H, Fujiwara Y, Hashimoto K, Maoka T, *et al.* An antitumor promoter from *Moringa oleifera* Lam. Mutat Res. 1999;440(2):181-8. doi: 10.1016/s1383-5718(99)00025-x, PMID 10209341.
83. Screening of antihistaminic activity of *Fagonia schweinfurthii* Hadidi in guinea pig ileum and formulate antihistaminic syrup.
84. Romde RR, Ningwal M, Kaurav RK. Antihistaminic activity of *Euphorbia hirta* extract on asthmatic rats. Int J Adv Pharm Biol Chem. 2014;3(2):434-6.

Cite this article: Maldhure PG, Wanjari A, Naharwal K. Exploring Herbal Antihistaminics-Natural Allergy Fighters for Comprehensive Health Care. Int. J. Pharm. Investigation. 2025;15(1):10-8.