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A Comprehensive Study on Some Reported Polyherbal Formulation with Potential Antihistaminic activity

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ABSTRACT

The polyherbalism that is a combination of two or more herbs expresses the fundamental aspect of Ayurvedic/herbal drug formulation. As per the many pieces of evidence shows the various herbal formulation with different potency acts by a unique mechanism. By which the Polyherbal formulation today make the choice for threatened disease or disorder rather than single one, to gain synergistic therapeutic application. The allergens produce immunoglobulin E (IgE)-mediated immune response and instant hypersensitivity reaction result in asthma, hay fever, atopic dermatitis, allergic rhinitis, food, and drug-induced allergies. Taking into consideration the etiology of upper respiratory tract infection, nowadays antihistamines are the choice of drug for the treatment of viral infections of the upper respiratory tract can be practice to stop complex inflammatory mediated reaction mainly effective in adult patients. The different plant species are discovered and applied over various clinical manifestations related to an allergic response. According to the traditional system of medicine, common plant species with their plant part used in some Antihistaminic Polyherbal formulation were assessed by Animal model work on the allergic response which includes HK-07, Unani eye drop, Bharangyadi, Ashmi, Pentapala-04. This study proved that many herbs combination has anti-histaminic and anti-allergic activity.

Keywords: Traditional medicine system, Polyherbalism, Allergy, Anti-Histaminic.

INTRODUCTION

Since the ancient period, herbal medicines used for their therapeutic applications cured several diseases. They were used in ancient Indian medicine for various therapies purposes. The Indian Ayurvedic Medicine system has included plants as one of its most powerful healing ingredients, which are recorded earlier in the literature such as Samhitas and Vedas.

After a long history in formulation of herbal drug emerge the desired effect in combined drug rather than single. The combination of two or more herbs regarded as polyherbalism and their formulation as Polyherbal formulation. The polyherbalism express the fundamental aspect of Ayurvedic / herbal drug formulation. The concept of synergism to polyherbal formulations entitle by Sarandghar Samhita. The herbs in combination are chosen according to disease or disorder as shows the peculiar therapeutic activity by synergism. In such Polyherbal formulation may other herbs are used to prevent side effects arising from the principal herb. So as per the many evidences shows the various herbal formulation with different potency act by a unique mechanism. By which the Polyherbal formulation today make the choice for threatened disease or disorder rather than single one, to gain synergistic therapeutic application ^[1].

Due to the modernization in scientific study today, the number of therapeutically potential polyherbal formulation has been identified. The present phytoconstituents, such as alkaloids, tannins, saponins, phenolic compounds, flavone, flavonoids, glycosides, terpenoids, and sesquiterpenes lactones of herbs leads to potency of the chosen herbal combination.

By a study it shows that, an individual herb contains more than one of the aforementioned phytochemical constituents are of generally same Chemical and Pharmacological value, which works synergistically with each other in producing pharmacological action ^[2].

Many plants are used utterly for medicinal purposes useful to mankind. According to the World Health Organization (WHO), "a medicinal plant is a plant which, in one or more of its organs, contains substances that can be used for therapeutic purposes, or which are precursors for chemo-pharmaceutical semi-synthesis" ^[3, 4]. Many Plants have been used in traditional medicines for the different ailment. And

And even today World's residents rely only on potential plants as their source of drug. India has sole wealth of medicinal plants and old traditional knowledge of utilization of herbal medicine [5].

What is Allergy?

The allergens are the Substances that can cause allergic reactions. They are may be dust, pollen grains, mites, mold spores, cosmetics and food. The allergic response results in asthma, hay fever, atopic dermatitis, allergic rhinitis, food and drug-induced allergies by immunoglobulin E (IgE)-mediated immune response and instant hypersensitivity reaction. [6] According to how long lasting symptoms on body, Allergy shows symptomatic difference with Cold as shown in figure 1.

When an allergen crosses through outer surface of skin in the body, an antigen-presenting cell digests the allergen and introduces presenting cell to a T cell. The T cell differentiates into a Th1 cell, which interacts with B cell to release cytokines, can cause to differentiate into a plasma cell. The plasma cell will start producing IgG antibodies. And they help to destroy the allergens without causing an allergic response. If the T cell differentiates into a Th2 cell in its place of IgG the plasma cell will produce IgE antibodies. For the next time if allergen enters in the body, the IgE's recognize the allergen, called sensitization as shown in figure-2.

Histamine plays an important role in human physiology, influencing acute and chronic inflammatory response through different types of receptors (H1, H2, H3, and H4). Apart from all histaminic receptors, histamine also blocks adrenergic, dopaminergic and muscarinic receptors, causing cardiovascular, urinary and gastrointestinal adverse reactions. The clinical symptoms of allergic rhinitis which is complex inflammatory reaction include nasal congestion, rhinorrhea, sneezing and itchy nose caused by contact with allergens as shown in figure-3. It shows clinical symptoms include concentration disturbance, fatigue, or snoring [7, 8].

Allergic conjunctivitis is also another inflammatory response coincides with allergic rhinitis by symptoms including redness and itching of cornea, watering [9]. Urticaria showing a symptom include erythema, oedema, burning sensation also been related to antihistaminic treatment. And for that only Histamine is responsible as basic mediator [10, 11].

Taking into consideration the etiology of upper respiratory tract infection, nowadays antihistamines are choice of drug for treatment of viral infections of the upper respiratory tract can be practice to stop complex inflammatory mediated reaction mainly effective in adult patients [12].

The different plant species are discovered and applied over various clinical manifestations related to allergic response. According to traditional system of medicine, common plant species with their plant part used in some Antihistaminic Polyherbal formulation which are listed below in table-01:

Antihistaminic Polyherbal formulation:

In this present review article, an attempt was made to list out the diverse Polyherbal formulation possessing Antihistaminic activity by one or the other possible mechanisms. The different formulation was assessed by Animal model work on allergic response which are include HK-07, Unani eye drop, Bharangyadi, Ashmi, Pentapala-04 in Table 2.

A] HK-07

HK-07 is a polyherbal combination containing extracts of *Cyperus rotundus*, *Curcuma longa*, *Piper longum*, *Adhatoda vasica*, *Zingiber officinale*, *Emblca officinalis*, *Ocimum sanctum*, *Terminalia belleric*. The individual therapeutic indications are given in the Table-3.

S. Gopumadhavan et.al was evaluated HK-07 combination using Wistar rats and Duncan Hartley guinea pigs. By using the active anaphylaxis model, Antianaphylactic activity was investigated in rats. HK-07 shows prolonged the latent period of Preconvulsive Dyspnea (PCD) in guinea pigs subsequent histamine aerosol. This concludes the Antihistaminic activity of HK-07. The HK-07 offered protection against Anaphylactic shock induced bronchospasm in rats. In this study HK-07 has shown noticeable protection against the mast cell degranulation in sensitized animals. The presence of seven herbal extract in HK-07 gives Mast cell stabilizing activity by showing antigen-antibody reaction due to suppression of IgE Antibody production which is responsible for mast cell degranulation. The suppression of IgE, inhibition of pathological effects and stabilization of the mast cell membrane conclude anti anaphylactic and antihistaminic effect to the HK-07 formulation by the release of inflammatory mediators.

The ex-vivo effect on mast cell stabilization was performed on antigen in sensitized rat intestinal mesenteries. By using histamine-induced bronchospasm in guinea pigs was studied for Antihistaminic activity. The Dose-response studies were conducted at 125, 250, and 500 mg/kg in anaphylactic shock-induced bronchospasm in rats on HK-07 formulation [23].

a) Effect of HK-07 on Anaphylactic Shock-Induced Bronchospasm in Sensitized Rats

In a dose-dependent manner, the seven different medicinal plant extract in HK-07 polyherbal formulation protected the sensitized Wistar rats against anaphylactic shock. In control rats, intravenous antigen challenge (horse serum) caused shock in 100% of the animals, while in treated rats (500 mg/kg of HK-07), the onset of symptoms of shock was delayed, and symptoms were less severe with reduced mortality.

b) Mast Cell Stabilizing Potential of HK-07

Antigen challenge resulted in considerable degranulation of the approximately 88% mesenteric mast cells. When challenged with horse serum, with HK-07 in a Pretreatment dose of 500 mg/kg to sensitized animals for 2 weeks shows a significant reduction in the number of mast cells that were disrupted. The effect of HK-07 was compared with prednisolone as a reference drug.

c) Effect on Histamine-Induced Bronchospasm

As compared to control, HK-07 at 500 mg/kg appreciably prolonged the latent period of PCD, subsequently exposure to histamine aerosols on day 5 [23].

B] Unani eye drop

The Unani eye drop is an ophthalmic formulation was prepared by Latif Abdul and et. al. for its anti-inflammatory and antihistaminic activity. The Unani eye drop was prepared by combining *Berberis aristata*, *Cassia absus*, *Coptis teeta*, *Symplocos racemosa*, *Azadirachta indica*, Alum and distillate of *Rosa damascene*. There is a dearth of commercial Unani ocular preparations because of the less availability of literature and Unani clinical practice has effectively in treatment of eye diseases by various Unani physicians. Thus, the formulation of eye preparations becomes imperative to bring the anti-inflammatory activity of various indigenous drugs. The Latif Abdul and et. al. brings these indigenous drugs to the front foot and evaluate their activities in view of the importance of alternative anti-inflammatory and antiallergic drugs. The individual therapeutic indications are given in the Table 4.

The beneficial effects of Unani eye drop against the inflammatory and allergic conditions of the eyes and investigated using *in vivo* experimental models for anti-inflammatory activity and *in vitro* antihistaminic activity. The Latif Abdul and et. al. exhibited significant anti-inflammatory activity ocular inflammation in rabbits induced by turpentine liniment. And also showed considerable antihistaminic

activity on ileum isolated from guinea-pig. This eye drop having strong anti-inflammatory and antihistaminic activity may be due to presence of active ingredients in the formulation. When compared with that of control group, The Unani ophthalmic solution gave significant effect when the effect was comparable to that of Flurbiprofen ophthalmic solution. When tested Unani eye drop formulation is compared to that of potent anti-inflammatory ophthalmic eye drop, flurbiprofen sodium reveal the usefulness in the treatment of conjunctiva and the tested Unani eye drop also exhibited superior antihistaminic effect antagonize the effect of histamine on isolated guinea pig ileum proved to possess a potent anti-inflammatory and antihistaminic activity [24].

C] Bharangyadi

Divya Kajaria et.al. combine different indigenous drugs aimed to act against Bronchial asthma which is an airway chronic inflammatory disorder. They investigate such Polyherbal formulation to show good anti-asthmatic activity by formulating such polyherbal combination having Bharangi (*Clerodendrum serratum*), Sati (*Hedychium spicatum*) and Pushkarmoola (*Inula racemosa*) as ingredient herbs named as Bharangyadi. The individual therapeutic indications are given in the Table 5.

As the physiology said that a causal relationship may exist between airway inflammation and airway hyperresponsiveness. The release of histamine as inflammatory mediators in responsive with the attachment of the antigen-antibody complex to the mast cell causes its disruption. The evaluation of mast cell stabilizing property, anti-histaminic activity and bronchodilator property used as pharmacodynamic parameters to prove the efficacy of anti-asthmatic property of a drug. Divya Kajaria et.al. aimed to study and evaluate the anti-asthmatic activity through various in-vitro & in-vivo experimental models for an indigenous polyherbal compound Bharangyadi. The Bharangyadi, polyherbal compound demonstrate that Ethanolic extract of drug with significant spasmolytic activity and mast cell stabilizing activity in the experimental animals. Bharangyadi, a potent mast cell degranulator, provoked 76% degranulation of mast cells in the control group in a dose-dependent manner. The drug reduces the smooth muscle contraction resulting through Screening of Histamine antagonism activity on guinea pig ileum in a dose-dependent manner. Increasing concentration of Bharangyadi extract with the maximum dose of histamine (1.6µg) showed maximum inhibition at the dose of 50mg (99.78%). [25]

D] ASHMI

The Bolleddula Jayaprakasam, Nan Yang and et. al. was designed a study to determine synergistic exhibition of the anti-inflammatory effects of individual herbal constituents of ASHMI.

ASMI is a combination of three traditional Chinese medicinal herbs which are the Fruiting body of Lingzhi (*Ganoderma lucidum*), dried Roots of Kushen (*Sophora flavescens*) and dried Roots of Gancao (*Glycyrrhiza uralensis*) showed Anti-asthma herbal medicine intervention. The Effects of aqueous extracts of Lingzhi (*Ganoderma lucidum*), Kushen (*Sophora flavescens*) and Gancao (*Glycyrrhiza uralensis*), on eotaxin-1 secretion by human lung fibroblast (HLF-1) cells and Th2 cytokine secretion by murine memory Th2 cells were determined by measuring levels in culture supernatants by enzyme linked immune sorbent assay (ELISA). By computing interaction indices from concentration-effect curve parameters, Potential synergistic effects were determined. [26] The individual therapeutic indications are given in the Table 6.

E] PENTAPALA-04

Pentapala-04 is the aqueous extract of five medicinal plants tested against ova albumin and aluminium hydroxide induced lung damage in rats found to be more effective by showing increased Lung Body-Weight Index (LBI) and decreased lung lipid content which might be due to the protective activity of all five plants which are *Adhatoda vasica*, *Ocimum sanctum*, *Coleus aromaticus*, *Glycyrrhiza glabra*, *Alpiania galangal*. [27] The individual therapeutic indications are given in the Table 7.



Figure 1: Symptomatic difference in Allergy and Cold

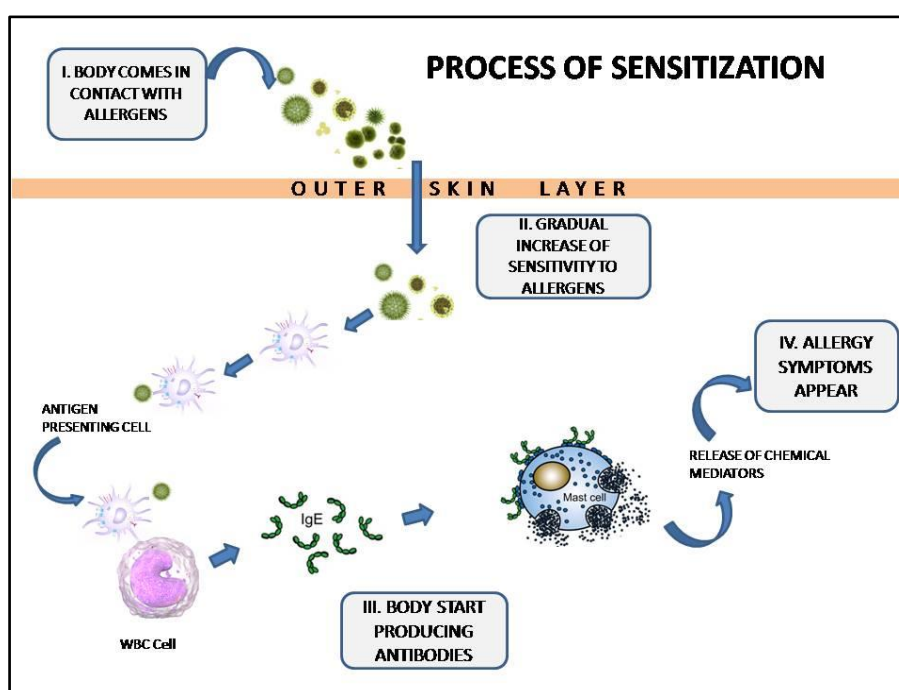


Figure 2: Process of Sensitization

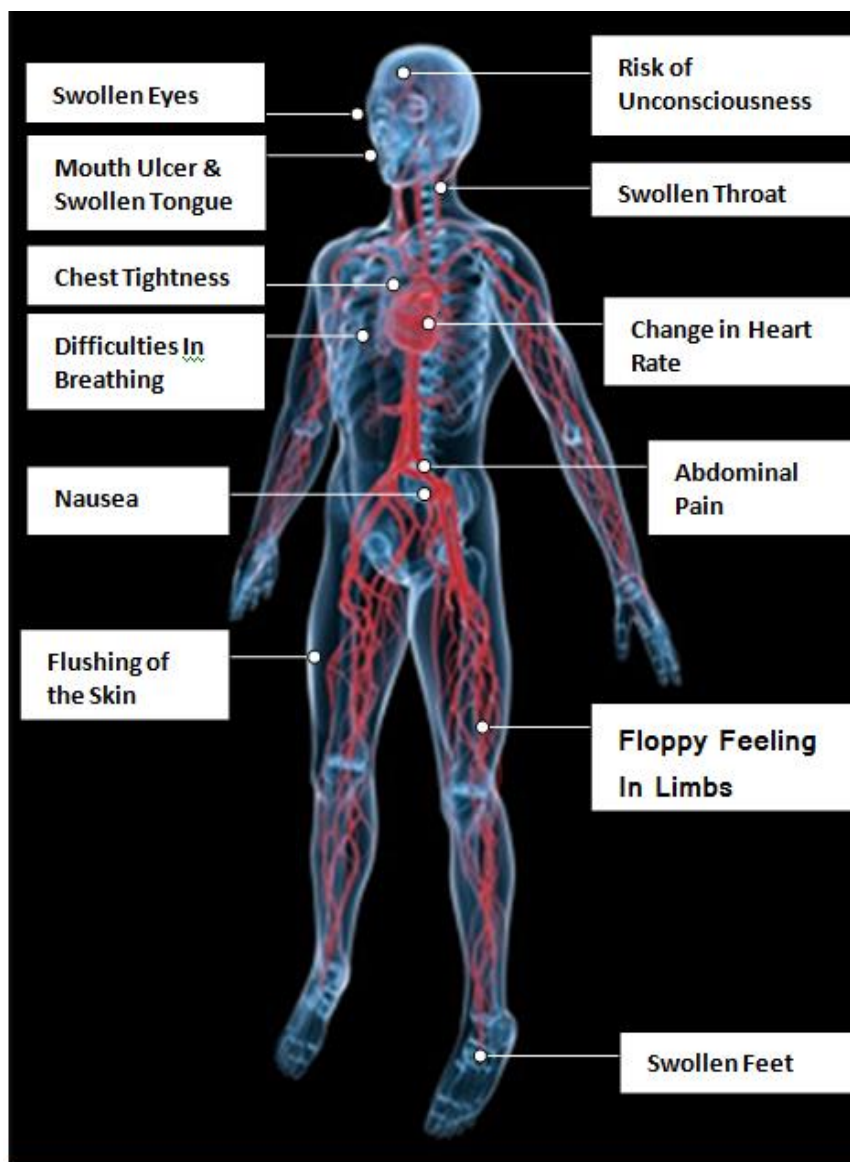


Figure 3: Symptomatic difference in Allergy and Cold

Table 1: Commonly Used Some Antihistaminic Herbs in Herbal Formulation

Sr. No.	Botanical Name	Family	Common Name	Part used
1	<i>Curcuma longa</i> [13]	Zingiberaceae	Turmeric	Rhizome
2	<i>Cyperus rotundus</i> [14]	Cyperaceae	Nagarmotha	Tuber
3	<i>Zingiber officinale</i> [15]	Zingiberaceae	Ginger	Rhizome
4	<i>Allium cepa</i> [16]	Liliaceae	Garlic	Bulb
5	<i>Emblia officinalis</i> [17]	Phyllanthaceae	Amla	Fruit
6	<i>Piper longum</i> [18]	Piperaceae	Indian long pepper or pipili	Fruit
7	<i>Ocimum sanctum</i> [19]	Lamiaceae	holy basil or tulsi	Leaves
8	<i>Azadirachta indica</i> [20]	Meliaceae	Neem	Leaves, Seed
9	<i>Adhatoda vasica</i> [21]	Acanthaceae	adulsa, adhatoda	Leaves
10	<i>Berberis aristata</i> [22]	Berberidaceae	Indian barberry	Root

Table 2: Polyherbal Formulation Along with the Different Pharmacological Activities

Polyherbal formulation	Composition	Established by
HK-07[23]	<i>Curcuma longa, Zingiber officinale, Piper longum, Emblica officinalis, Terminalia belerica, Ocimum sanctum, Adhatoda vasica, Cyperus rotundus</i>	Active anaphylaxis model in rats and histamine-induced in guinea pigs
Unani eye drop [24]	<i>Berberis aristata, Cassia absus, Coptis teeta, Symplocos racemosa, Azadirachta indica, Alum and distillate of Rosa damascene</i>	Isolated guinea pig ileum
Bharangyadi [25]	<i>Clerodendrum serratum, Hedychium spicatum, Inula racemosa</i>	Histamine induced model
Ashmi [26]	<i>Ganoderma lucidum, Sophora flavescens, Glycyrrhiza uralensis</i>	Th2 cytokine secretion, Eotaxin -1 secretion
Pentapala-04 [27]	<i>Adhatoda vasica, Ocimum sanctum, Coleus aromaticus, Glycyrrhiza glabra, Alpinia galangal</i>	Al(OH) ₃ induced lung damage

Table 3: Therapeutic Indications of Medicinal Plant Taken in Hk-07 Formulation

Name of Medicinal Plant	Part Used	Major Chemical Composition
<i>Cyperus rotundus</i>	Fruit	Cyperene, Humulen, Selinene, Zierone, Campholenic
<i>Curcuma longa</i>	Rhizome	Polyphenolic compounds as Curcuminoids, which contain of Curcumin, Bisdemethoxycurcumin and Demethoxycurcumin.
<i>Piper longum</i>	Fruit	Piperine, Chavicine, Piperanine, Isochavicine, Isopiperine and Coumaperine.
<i>Adhatoda vasica</i>	Leaves	Vasicine, Essential oil contain 1, 2, 3-Trimethyl Benzene, Borneol, Ethanonaphthalene, Alphacaryophyllene, Caryophyllene Oxide.
<i>Zingiber officinale</i>	Rhizome	Limonene, β-Zingiberene, Neral, 1, 8-Cineole, β-Phellandrene, Geraniol, β-Bisabolene, β-Sesuihellandrene.
<i>Ocimum sanctum</i>	Leaves	71% Eugenol, 20% Methyl Eugenol, Oleanolic Acid, Linalool, Ursolic Acid, Rosmarinic Acid, Apigenin, Carvacrol, B-Caryophyllene, Circimaritin, Isothymusin.
<i>Terminalia beleric</i>	Fruit	Ellagic Acid, Ethyl Gallate, β- Sitosterol, Galloyl Glucose, Gallic Acid, Corilagin And Chebulaginic Acid.

Table 4: Therapeutic Indications of Medicinal Plant Taken in Unani Eye Drop Formulation

Name of Medicinal Plant	Part Used	Major Chemical Composition
<i>Berberis aristata</i>	Roots	Xyacanthine, Berberine, Jatrorrhizine, Berbamine, Berberrubine, Oxycanthine, Columbamine, Isotetrandrine, Palmatine.
<i>Cassia absus</i>	Seeds	Palmitic, Luteolin, Stearic And Arachidic Acids
<i>Coptis teeta</i>	Rhizome	Palmatine Jatrorrhizine, Berberine, Columbamine, Coptisine And Epiberberine
<i>Symplocos racemosa</i>	Bark	Colloturine, Loturine, Linoleic Acid, Loturidine, Salireposide, Betasito-Glycoside, Symplocososide.
<i>Azadirachta indica</i>	Leaves, Seeds	Nimbin, Nimbolinin, Nimbidol, Nimbidin, Salannin, Sodium Nimbinatate and Quercetin.
Alum	-	Potassium Aluminum Sulfate
Distillate of <i>Rosa damascene</i>	Flower	Nerol, Citronellol, Geraniol, A-Guaiene, Eicosane, Phenyl Ethyl Alcohol, Nonadecane, Nonadecene, Heneicosane, Tricosane, Geranyl Acetate And Eugenol

Table 5: Therapeutic Indications of Medicinal Plant Taken in Bharangyadi Formulation

Name of Medicinal Plant	Part Used	Major Chemical Composition
<i>Clerodendrum serratum</i>	Leaves	Cleroflavone, D-Mannitol, Hispidulin, Acteoside, Scutellarein, Verbascoside, Serratagenic Acid, Clerodermic Acid, Sitosterol.
<i>Hedychium spicatum</i>	Rhizome	1,8-Cineole, Linalool, A-Terpineol, B-Eudesmol, A-Selinene, Elemol, B-Selinene, A-Cadinol.
<i>Inula racemosa</i>	Rhizome and Roots	B-Sitosterol, Alantolactone, Inulin, Isoalantolactone, Dihydroalantolactone.

Table 6: Therapeutic Indications of Medicinal Plant Taken in Ashmi Formulation

Name of Medicinal Plant	Part used	Major Chemical Composition
<i>Ganoderma lucidum</i>	Stalk of Mushroom	D-Asparagic acid, Glycin, Tryptophan, Arginine, L-Alanine, L-Serine, L-Threonine, Glutamic acid, Methionine, Proline, Leucine, Tyrosine and Phenylalanine.
<i>Sophora flavescens</i>	Roots	Oxymatrine
<i>Glycyrrhiza uralensis</i>	Roots	Liquiritin, Isoliquiritin and Liquiligitenin.

Table 7: Therapeutic Indications of Medicinal Plant Taken in Pentapala-04 Formulation

Name of Medicinal Plant	Part used	Major Chemical Composition
<i>Adhatoda vasica</i>	Leaves	Vasicine, Essential oil contain 1, 2, 3-Trimethyl Benzene, Borneol, Ethanaphthalene, Alphacaryophyllene, Caryophyllene oxide.
<i>Ocimum sanctum</i>	Leaves	71% Eugenol, 20% Methyl Eugenol, Oleonic acid, Linalool, Ursolic acid, Rosmarinic acid, Apigenin, Carvacrol, β -Caryophyllene, Circimaritin, Isothymusin.
<i>Coleus aromaticus</i>	Roots	Eugenol, Carvacrol, Chavicol, Thymol, Ethyl Salicylate
<i>Glycyrrhiza glabra</i>	Roots	Liquirtin, Isoliquertin Liquiritigenin, Rhamnoliquirilin, Shinflavanone, Glucoliquiritin Apioside, Prenyllicoflavone A, Shnpterocarpin and 1-Metho-Xyphaseolin.
<i>Alpiania galangal</i>	Rhizome	Essential oil contains Eucalyptol, β -Pinene, α -Pinene, α -Terpineol and Borneol followed by Camphor and Camphene.

CONCLUSION

The scientific developments carry with perfection in Polyherbal formulation by study of principal chemical constituents and discovery of important plant combination, which work synergistically to give desirable effect. This study proved that many herbs combination have anti-histaminic and anti-allergic activity. In Allergic condition, medicines are taken for long duration and may get worse the pathology. There are many plants reported that for antiinflammatory properties which are found that having anti-histaminic activity evaluated *in-vivo* in animal models. Those plants in combination will produce synergistic action. In this review, the Antihistaminic Polyherbal formulations clearly demonstrate the potential efficacy of herbal plants as antiallergic action by mast cell stabilizing activity. So, Herbs with effortless availability, cost efficient, high significance and least side effects give an opportunity for explore and expect for complete cure of Allergic diseases. Hence, different Antihistaminic Polyherbal formulation reported in this review clearly reveal the importance of herbs in the treatment of various types of allergies and also to consider one of the safe and effective in inflammatory and allergic conditions were it can be used globally may be used as an alternative to synthetic drugs.

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