JPR INFO
Journal of Pharma Research

Journal of Pharma Research
Available online through
www.jprinfo.com

Research Article
ISSN: 2319-5622

Preclinical Evaluation of Polyherbal Formulation Consisting various Indigenous Plants for their Antiasthmatic Activity

S. S. Patil[1]*, Chandrawadan Vishwambhar Panchal [1], Bhagwat Nivrithirao Poul[1], Mallinath Maruti Langde[2], Mahesh Dattatraya Burande[3]

*[1]Maharashtra College of Pharmacy, Nilanga, Dist. Latur, PIN-413521, INDIA.
[2]Jawahar Mahavidyalaya, Andur, Tq. Tuljapur, Dist. Osmanabad, INDIA.
[3]Siddhant College of Pharmacy, Sadumbre, Dist. Pune, INDIA.

Received on: 17-07-2015; Revised and Accepted on: 09-08-2015

ABSTRACT

Literature survey revealed that the child own set and adult own set asthma increases progressively. About 20-40 5 population suffers from asthma. The available allopathic therapy is not safe in both the cases. Hence it is today's need to use herbal formulation to treat asthma to reduce untoward effect. In present study herbal formulation containing Passiflora incarnata, Picrorrhiza kurroa , Glycyrrhiza glabra and Ephedra sinica have been prepared and evaluated for antiasthmatic activity by using experimental animals. This preclinical study revealed that from the different doses of above formulation the dose 1500mg/kg shows significant effect in different screening models. The asthmatic effect can be potentiated by using multiple herbal drugs or by isolating the phytoconstituents from this indigenous plant material.

Keywords: *Asthma, Preclinical study, Hyper Response, Polyherbal Formulation.*

INTRODUCTION

Bronchial asthma is characterized by hyper-responsiveness of trachea-bronchial smooth muscle to a variety of stimuli, resulting in narrowing of air tubes, often accompanied by increased secretions, mucosal edema and mucous plug-in.

Asthma is now recognized to be a primarily inflammatory condition/inflammation underline hyperactivity. An allergic basis can be demonstrated in many adult and higher percentage paediatric patients. In others, a variety of trigger factors (infection, irritants, pollution, exercise, exposure to cold air, psychogenic) may be involved.

Approaches to treatment: [1]

Prevention of antigen antibody reaction – avoidance of antigen, hypo sensitization- possibly in extrinsic asthma and if antigen can be identified.

Suppression of inflammation and bronchial hyperactivity – corticosteroids.
Prevention of release of mediators – mass cell stabilizers
Antagonism of released mediators - leucorine antagonists, antihistamines, PAF antagonists.
Blockage of constrictor neurotransmitter – anticholinergics.
Mimicking dilator neurotransmitter – sympathomimetics.
Directly acting bronchodilators – methyl xanthenes.

The present study validates the use of Polyherbal drugs for the curative treatment of asthma. Scientific literature showed that the present available allopathic therapy for the treatment of asthma showed serious adverse reactions. Hence the use of Polyherbal drugs is todays need to treat asthma. In present study formulation consist four different herbal plants viz Leaves of Passiflora incarnata, roots of Picrorhiza kurroa, stolons of *Glycyrrhiza glabra*, stem of *Ephedra sinica*. The different pharmacological screening models have been used to evaluate the formulation.

***Corresponding author:**
Prof. (Dr.) S. S. Patil
Professor & Head, Department of Pharmacology
Maharshtra College of Pharmacy, Nilanga, Dist. Latur. INDIA.
Cell No. 9404348788.
**E-Mail: patil_ss12@rediffmail.com*

MATERIALS AND METHODS

Table No. 1: List of drugs used in the study.

Drugs	Company
Histamine diphosphate	Sigma Aldrich, India.
Clonidine	Unichem, India.
Dexamethasone	Cadila Healthcare Ltd, India.
Chlorpheniramine Maleate	Research Lab Fine Chem., India.
Egg albumin	Burgoyne Burdidges company, India.
Sodium cromoglycate	Cipla Laboratory, Goa, India.
RPMI 1640 buffer medium	HiMedia Lab.Pvt.Ltd. Mumbai.
Mepyramine	Purchased from local market.

Table No. 2: List of chemicals used in the study.

Name of Reagent	Company
Eosin solution	Qualigens, India
Toluidine Blue	Research Lab Fine Chem., India.
WBC Diluting fluid	Qualigens, India

The chemicals used for physiological salt solutions and other preparations were of analytical grade.

Plant material:

All the plants/parts were identified and authenticated at Department of Botany, University of Pune, Pune and Voucher specimen *Passiflora incarnata* -SSP1, *Picrorrhiza kurroa* - SSP2, *Glycyrrhiza glabra* - SSP3, *Ephedra sinica*- SSP4 were kept as specimen.

Preparation of extract:

All the four medicinal plants were subjected to aqueous extraction through maceration at room temperature. The extract was then filtered through filter paper, dried and stored [2].

Preparation of drug solution:

Accurately weighed quantities of the powdered extracts were dissolved in distilled water to prepare required formulation. These formulations were stored in the refrigerator.

Route of administration:

The above prepared Polyherbal formulation was administered by oral route to respective groups using oral feeding needle no 18. Chlorpheniramine maleate, Dexamethasone and Sodium cromoglycate was injected by intraperitonial route. Clonidine was injected by the subcutaneous route.

Animals:

Dunkin-Hatley Guinea pigs weighing 350-400g of either sex, wistar albino rats (120-150 gm) and albino mice (30-50gm) were procured from central animal house Maharashtra College of Pharmacy, Nilanga, District Latur. They were maintained at 25 ± 2° C and relative humidity of 45 to 55% and under standard environmental conditions (12 h light: 12 h dark cycle). The animals had free access to food (Amrut feed, Chakan oil mills, India) and water ad libitum throughout study. Institutional Animal Ethical Committee approved the protocol. All the experiments were carried out between 9:00- 16:00 hours.

Acute toxicity test:

Acute toxicity study was performed in healthy albino mice (30-50gm) as per guidelines (AOT 425) suggested by the Organization for Economical Co-operation and Development (OECD).

Polyherbal Formulation was administered to the mice for oral toxicity study. These mice were then observed for incidence of mortality or any sign of toxicity up to 24 hours after oral administration.

The dosing schedule as per the OECD (guideline 425) was as follows: Only one mouse received a dose at a particular time. First mice received a dose of 175 mg/kg and were observed for 03 hours after dosing for any toxicity signs, survival or death. If the first animal died or appeared moribund, the second animal received a lower dose. The dose progression **or** reduction factor was 3.2 times of the previous dose. If no mortality was observed in the first animal then the second animal received a higher dose. Dosing of the next animal was continued depending on the outcome of the previously dosed animal for a fixed time interval (03 hours). The test was stopped when one of the stopping criteria was met:

- 05 reversals occur in any 06 consecutive animals tested.
- 03 consecutive animals died at one dose level.

Survived animals were observed for outcomes for a period of 24 hours (AOT425 Guidelines).

Methods for Anti-Asthmatic Activity:

Table No. 3: Grouping and treatment

Group No	Treatment	Dose
Group No. 1	Control (Distilled water)	10 ml/kg, p.o.
Group No. 2	Formulation Dose	500 mg/kg, p.o.
Group No. 3	Formulation Dose	1000 mg/kg, p.o.
Group No. 4	Formulation Dose	1500 mg/kg, p.o.

Passive Paw Anaphylaxis in rats: [3]

Preparation of serum for sensitisation:

1. Anti serum to egg albumin was raised in rats using aluminum hydroxide gel as an adjuvant.
2. Animals were given three doses of 100 µg (s.c.) of egg albumin adsorbed on 12 mg of aluminum hydroxide gel, prepared in 0.5 ml of saline on 1st, 3rd and 5th day.
3. On 10th day of sensitisation, the blood was collected from the retro orbital plexus, allowed to clot and the serum was separated by centrifugation at 1500 rpm.

Procedure:

1. 24 albino rats of wistar strain were randomly divided into 04 groups each containing 06 rats. These animals were passively sensitised with 0.1 ml of the undiluted serum into the left hind paw. The opposite paw received an equal volume of saline.
2. 24 hours after sensitisation these animals were given the drug treatment as shown in Table no. 4.4.
3. 01 hour after treatment of test and reference standard drug, the animals were challenged in the left hind paw with 10 µg of egg albumin in 0.1 ml of saline, and the paw inflammation was measured as volume of displacement in ml at interval of 01, 02, 03 and 04 hours using a digital Plethysmometer.

Histamine induced Bronchoconstriction in Guinea pigs: [4]

Procedure:

1. 24 overnight fasted guinea pigs were randomly divided into 04 groups each containing 06 animals.
2. Prior to drug treatment each animal was placed in the histamine chamber and exposed to 0.2 % histamine aerosol.
3. The latency of dyspnea (i.e from the time of exposure leading to the appearance of preconvulsion dyspnea) (PCD) was determined. As soon as the PCD was noted, the animal was removed from the chamber and placed in a fresh air.
4. 24 hours later the animals were treated as shown in Table No. 4.5.
5. These animals were again subjected to histamine aerosol later at interval of 01 hour, 04 hours and 24 hours of drug administration and latency of dyspnea was determined at each interval.

Clonidine-induced catalepsy in mice: [5]

Procedure:

1. Bar test was used to study the effect of test drug on clonidine-induced catalepsy in mice.
2. 24 albino mice were randomly divided into 4 groups, having 06 animals in each group and were treated as per Table No. 4.6. Chlorpheniramine maleate (10 mg/kg, i.p.), was used as the reference standard.
3. 01 hour after the drug administration, all the groups received clonidine (1 mg/kg, s.c.), and 45 minutes later the forepaws of mice were placed on a horizontal bar (1 cm in diameter, 3 cm above the table).
4. The time required to remove the paws from bar (i.e duration of catalepsy) was noted for each animal at 15, 30, 60, 90, 120, 150 and 180 minutes.

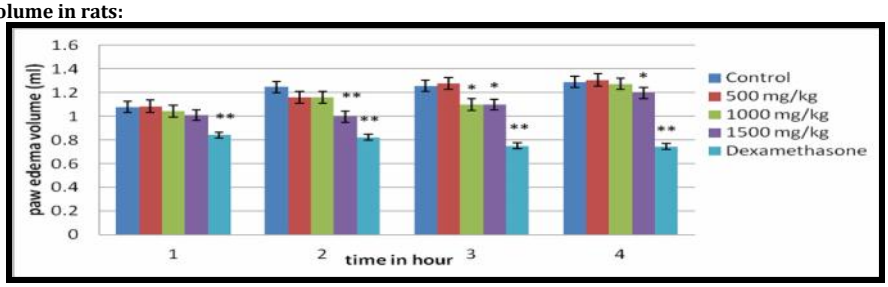
Milk-induced Leucocytosis and Eosinophilia in mice[6]

Procedure:

1. 24 albino mice were randomly divided into 04 groups with 06 animals in each group and were treated as per Table No 4.7.
2. 01 hour after the below mentioned treatment each animal was injected with milk (4 mg/kg, i.p).
3. Blood samples were collected from retro-orbital plexus and total leucocyte and eosinophil count was done in each group before the treatment and 24 hours after milk injection.
4. Difference in the count was then calculated.

RESULT

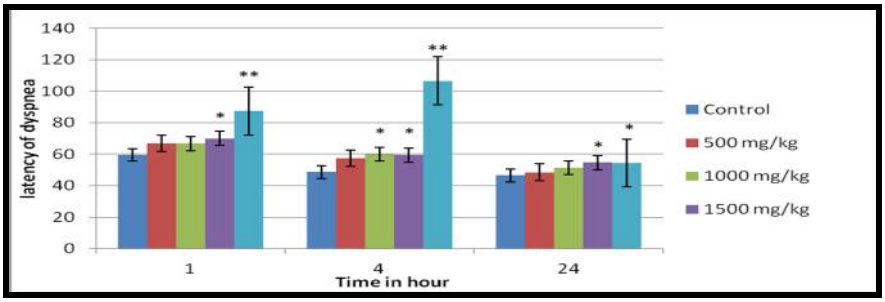
The paw edema volume in rats:



Results are expressed as mean ± SEM (n = 6). Data was analysed by using one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p < 0.01

Fig. 1: Effect of Polyherbal Formulation and Dexamethasone on the paw edema volume in rats

Chlorpheniramine maleate on latency of dysponea:



Results are expressed as mean ± SEM (n = 6). Data was analysed by using one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p< 0.05, ** p< 0.01, *** p< 0.001.

Fig. 2: Effect of Polyherbal Formulation and Chlorpheniramine maleate on latency of dyspnea in Histamine induced bronchoconstriction in guinea pigs

Clonidine induced catalepsy in mice:

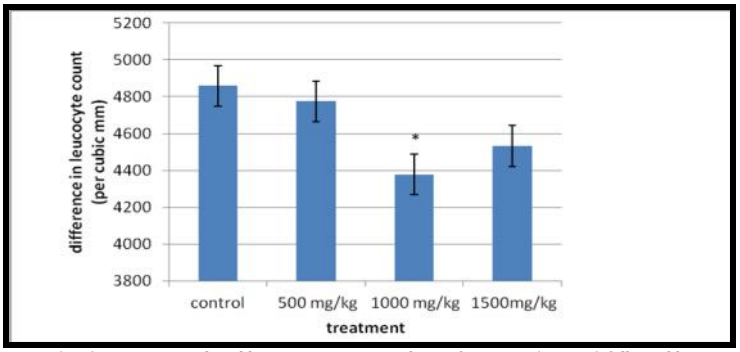
In case of Polyherbal Formulation, pretreatment with the dose of 1500 mg/kg was found to be highly significant (p<0.01) in reducing the duration of catalepsy only at all the interval of 90 minutes. It was also equally significant (p<0.05) at 30, 60, 120 and 150 minutes. The dose of 1000 mg/kg was found to be significant only at the intervals of 90, 120 and 150 minutes. It was more significant at 90 minutes (p<0.01) than 120 and 150 minutes (p<0.05). The dose of 500 mg/kg was insignificant in this regard.

Table No. 4: Effect of Polyherbal Formulation and Chlorpheniramine maleate on duration of catalepsy in mice

Polyherbal Formulation	Duration of catalepsy (min)						
	15 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	29.31± 0.90	82.95±1.87	202.46± 4.71	242.43± 4.13	278.12± 3.69	250.22±4.08	241.36±3.83
500 mg/kg	28.01± 1.05	77.28±1.68	199.69±4.34	234.63± 4.20	273.87± 2.19	246.65± 2.89	241.83±1.93
1000 mg/kg	27.99± 0.81	78.31±1.90	199.22±4.23	213.73**± 2.32	267.44*±2.59	238.49*±1.36	242.54±2.48
1500 mg/kg	27.95±1.06	75.25*±1.66	185.32*±1.97	211.41**± 3.34	266.84*± 1.89	238.82*±2.13	239.20± 1.95
Chlorpheniramine maleate	30.48±0.99	50.35**±1.11	66.26**±2.91	62.18**±3.30	2.13**± 2.66	123.61**±3.50	146.42**± 4.12

Results are expressed as mean ± SEM (n=6). Data was analysed by using one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p < 0.01

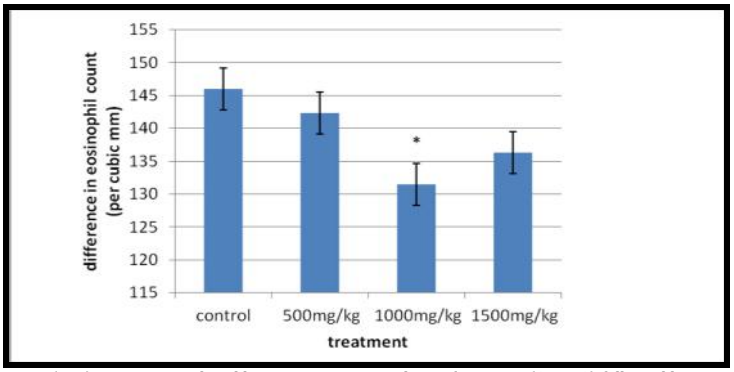
Milk-induced Leucocytosis in mice:



Results are expressed as mean ± SEM (n=6). Data was analysed by using one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Fig. 3: Effect of Polyherbal Formulation on Milk-induced Leucocytosis in mice

Milk-induced Eosinophilia in mice:



Results are expressed as mean ± SEM (n=6). Data was analysed by using one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p < 0.01

Fig. 4: Effect of Polyherbal Formulation on Milk-induced Eosinophil in mice

DISCUSSION

Asthma may be defined as syndrome in which there is current "reversible" obstruction of the airways in response to stimuli which are not in themselves noxious and which do not affect non asthmatic subjects. The asthmatic subject was intermittent attacks of dysponea (disorder of breathing), wheezing and cough. The dysponea consisting of difficulty in breathing out. It contracts with the obstructive airways disease which is not reversible. But note that the term "reversible" as applied to asthma needs to be qualified since it is only the only acute attack of dysponea i.e. reversible-the underline pathological change may not be reversible and indeed can progress. In acute sevier asthma (also known as asthmaticus) the airway obstruction causing the dysponea can take days to reverse, and in some cases it is not reversible at all and proves to be fatal.

There is also high prevalence of usage of alternative traditional system of medicines for the treatment of asthma [7]. Ayurveda, an Indian traditional system of medicine offers a unique insight into comprehensive approach to asthma management through proper care of the respiratory tract. More than 400 medicinal plant species have been used ethno pharmacologically and traditionally to treat the symptoms of asthmatic and allergic disorders worldwide. However the scientific documentation of these plants is relatively scanty. Hence there is a growing interest regarding for the preclinical evaluation of various plants used in traditional system of medicine [8, 9]. Such preclinical evaluation may direct drug discovery in a systematic way to come out with the ideal theory that may fill the blank spots of the modern medicine and its system [10] (Kumar and Parmar, 2003). Scientific documentations of various extracts have revealed that, individual extracts are not sufficient to produce the effect comparable to that of the synthetic drugs. Hence combination of various extracts leading to a polyherbal formulation is an ideal way to enhance the therapeutic effectiveness [11]. However such combination may lead to either synergism or sometimes may show antagonism hence exactly opposite results may be obtained. Based upon the scientific documentations and phytoconstituents reported, appropriate extracts of suitable part in prescribed concentrations can be mixed to get desired polyherbal formulations with certain predictable effects. These predictions later can be confirmed by preclinical evaluation. On the similar ground, we have made three different polyherbal formulations as per the standard formulas of Ayurvedic proprietary medicines [12-14] and evaluated for its suitability as an antiasthmatic therapy.

Since asthma has various precipitants and its occurrence can be taken place by various mechanisms, the formulation prepared needs to be effective in most of these conditions to get wide clinical applications [15]. Hence rather than restricting to one model, we have used battery of models.

In any polyherbal formulation, pharmacological action exerted by formulation is mainly governed by certain phytochemicals; hence preliminary phytochemical evaluation of all three formulations was carried out. The analysis of Polyherbal Formulation showed the presence of alkaloids, glycosides, flavonoids, phenolic compounds and volatile oils. The presence of these different constituents and its interaction with other same phytoconstituents may be responsible to alter the therapeutic profile of individual formulations. The overall presence of phytochemicals is in accordance with the previous published reports wherein antiasthmatic action was established [16, 17]. This further supports the selection of suitable plants.

Since pharmacological evaluation showed different levels of significance from formulation to formulation, it may be due to the presence of alkaloids in Polyherbal Formulation.

Although the individual constituents of the polyherbal formulations have been documented for its antiasthmatic effect without any untoward effects, however it is essential to test it again for its toxicity profile to establish its safety when used in combination (i.e. polyherbal combination). In light of this, the acute oral toxicity studies of all three formulations were carried out. Our findings indicated that all these formulations were found to be devoid of any serious toxic symptoms and no mortality was found up to the dose of 2000 mg/kg. Also, the administration of Polyherbal Formulation did not show any change in the alertness, touch response and locomotor activity. Formulation II showed reduction in alertness and touch response whereas; Polyherbal Formulation reduced all these three observations. These results satisfy the first requirement of safety pharmacology. Based on these results and pilot study, three different doses i.e 500 mg/kg, 1000 mg/kg and 1500 mg/kg were selected for the further pharmacological evaluation.

Antigen antibody reaction results in mast cell degranulation which is the first step of asthma, is manifested as bronchoconstriction (role of histamine and leukotriene) and inflammation (role of leucocytes and eosinophils) [18]. The stabilisation of mast cells can be the most important step towards prevention of precipitation of asthma. In case of passive paw anaphylaxis model of asthma, there is immunological stimulation by ova albumin and the antibodies raised against the antigen are injected locally into the paw of rat. Local antigen antibody reaction in the rat paw manifests into the inflammation and paw edema. In the present investigation, the formulation was investigated against passive paw anaphylaxis model so as to evaluate the immunomodulatory efficacy of the formulations to be useful in allergic asthma [19, 20].

Pretreatment with 1500 mg/kg of Polyherbal Formulation showed significant reduction in inflammation induced by ova albumin at all intervals. It is now well known that mast cells are extensively involved in the pathophysiology of bronchial asthma. This suggests the possible use of the dose of 1500 mg/kg of formulation I, towards the prevention of allergic asthma which may be attributed to its mast cell stabilizing property. Thus this formulation is suitable to be used as a preventive remedy which is the most important measure in case of possible exposure to allergens [21].

Although mast cell stabilisation is an ideal precautionary measure in asthma management, however, this may not be possible in all clinical cases. Many times degranulation takes place without prior notice and patient exhibits first clinical manifestation i.e bronchoconstriction. In such case, relief from bronchoconstriction becomes the primary objective of treatment. Histamine is one of the major inflammatory mediators in the immediate phase of asthma, causing the precipitation of bronchoconstriction. This further leads to airway hyper responsiveness and bronchial airway inflammation. Also, bronchoconstriction which is mediated by H_1 histaminic action is treated as a major symptom because long term bronchoconstriction leading to hypoxia may result into generalised hypo functioning which if untreated can become a syndrome with serious complications [22]. A study regarding involvement of H_1 and H_2 receptors done in experimental model of asthma using guinea pig documented prominent involvement of H_1 receptors. Since majority types of asthma showed the role of histamine via H_1 receptor, any new formulation to be used in asthma was tested for its H_1 antihistaminic properties [23].

In this study, Polyherbal formulation was investigated for its inhibitory effect against histamine induced bronchoconstriction. The study found that Polyherbal Formulation was most effective in this regard as it showed significant delay in the latency of dyspnea. It also showed dose dependent effects suggesting that the preparation is devoid of any interaction or side effects even at large doses. Since severity of asthmatic condition can drastically vary in a single person from season to season and place to place, hence an ideal formulation shall be effective at wider dose range without any dose dependant limitations. This preparation satisfies this particular aspect. Moreover, although it acts through inhibition of H_1 receptor, still it did not show any sedation as recorded during its toxicity test which perhaps could be the best outcome towards patient compliances compared to the present synthetic medication. Present Polyherbal Formulation has not only delayed the latency but this ability was sustained for a longer duration of time hence doses to be administered to provide protection round the clock in a particular season or during specific predictable exposure can be reduced to a greater extent [24, 25]. This is an additional benefit of this combination. The increased duration may be attributed to the synergistic combinations of phytoconstituents.

Clonidine induced catalepsy is another widely used model for evaluation of anti H_1 asthmatic activity. Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining normal posture. Clonidine, α-2 adrenoceptor agonist induces dose dependent catalepsy in mice, which is inhibited by H_1 receptor antagonist but not by H_2 receptor antagonist [26]. It is also been proved that pretreatment with L-histidine, a precursor of histamine, potentiated clonidine-induced catalepsy in dose dependent manner and different stages of catalepsy appear to be directly correlated with brain histamine content. Muley et al, showed that intracerebroventricular injection of histamine in conscious mice induced catalepsy, which was inhibited by H_1 receptor antagonist [27]. Dhanalakshmi et al, 2004 showed that extracts having antihistaminic or mast cell stabilising effect in turn antiasthmatic activity inhibit clonidine-induced catalepsy [28].

In case of Polyherbal formulation, the dose of 1000 and 1500 mg/kg were found to be significant in reducing the duration of catalepsy mediated by histamine release from mast cell at all intervals except 15 minutes. Dose of 500 mg/kg was significant only at the interval of 90 minutes as compared to vehicle treated control group. Earlier studies have shown that inhibition of mast cell degranulation and H_1 antihistaminic property are responsible to inhibit clonidine induced catalepsy. Present Polyherbal Formulation once again reported both these effects in this model. As discussed earlier patient friendly, non sedating formulations for a wide range of asthma is another major outcome.

Asthma is also manifested as a chronic inflammatory process occurring due to exposure of specific allergen resulting in the subsequent release of inflammatory mediators (eg: leucocytes, eosinophils). Hence, it is well reported that immunomodulating agents are useful in the treatment of allergic asthma by inhibiting the antigen-antibody (AG-AB) reaction and there by inhibiting the release of inflammatory mediators [29, 30].

In milk induced leucocytosis and eosinophil model, milk is considered to be an antigen, which on parenteral administration induces abnormal increase in total leukocyte count (TLC) which is termed as leucocytosis. Leukocytes release the inflammatory mediators like cytokines, histamine, and major basic protein and promote the ongoing inflammation. In the late phase, especially in the case of allergic asthma, eosinophils play role as an inflammatory cell. Eosinophil secretes mediators such as eosinophile cationic protein (ECP), eosinophile derived neurotoxin (EDNT), granulocyte macrophage colony stimulating factor (GM-CSF), tumor necrosis factor (TNF), and Prostaglandin (PG), which results in epithelial shedding, bronchoconstriction and promotion of inflammation in respiratory tract [32] (Ward et al, 2002). Hence, immunomodulating agents are useful in the treatment of allergy by virtue of inhibiting the antigen-antibody (AG-AB) reaction thereby inhibiting release of inflammatory mediators [33].

In Polyherbal Formulation, all doses were significant reducing the difference in leucocytosis count whereas dose of 1000 and 1500 mg/kg only were significant in reducing the difference in eosinophil count. Hence, results suggest significant immunomodulatory potential of Formulation I, which can be of great use towards control of inflammation and associated complications in allergic asthma.

In the present investigation, Polyherbal Formulation was found to be the most effective which could be again combination of anti allergic, immunomodulatory and anti-inflammatory activity of its constituents. In addition, previously established antistress action exerted by Ocimum sanctum [34] further potentiated antiasthmatic effect of the formulation by combating stress induced respiratory dysfunction which has been recognised as one of the precipitants of allergic asthma. In today's competitive life, there is a great increase in the stress and strain which further leads to immunological complaints, asthma being is one of these complaints [35]. Present Polyherbal Formulation can be the best treatment to control such stress induced aggravation for which there is no drug available in the modern therapy.

Although antihistaminic property of the Polyherbal Formulation is well established using different preclinical (in vivo) models however it is considered to be indirect method. The ex-vivo preparation is another tool to be used for further confirmation [36].

In the present investigation, the effect of Polyherbal Formulation on isolated goat tracheal chain was recorded by using Biopac system. The results showed good agreement with the earlier in vivo observations. The DRC of histamine showed right shift in the presence of Polyherbal Formulation in a dose dependent manner. The calculation of percent inhibition of response also reported significant antihistaminic action.

Asthma has become a major threat due to its specific link with genetic trait and appearance of newer allergens day by day [37]. In such situation avoidance of allergens, prophylactic drug treatment or symptomatic management are major options. Out of this, many times first option is practically impossible (eg: pollution or smoke as an allergen) hence prophylactic drug treatment is preferred almost in all cases of allergic asthma. However it is possible only when allergens are known and exposure is predictable. In case of unidentified allergens and unpredictable exposure immediate control of various clinical manifestations viz bronchoconstriction, inflammation etc is required. Here Polyherbal Formulation has shown its possible use as a prophylactic and as a symptomatic treatment. This is a valuable advantage as compared to synthetic medication wherein different drugs need to be administered for these phases of asthma. This possible use of Polyherbal Formulation at multiple stages of asthma may be attributed to appropriate combination of various components and their phytoconstituents that act synergistically [38].

CONCLUSION

The available allopathic formulations for the treatment of asthma significantly affects on immunomodulation and other pathophysiological functions of organs. The use of Polyherbal formulation for the treatment of asthma is today's need to eradicate symptoms of asthma with less undesirable effects. In present used Polyherbal formulation consists various indigenous plants which shows significant response in all screening models. Hence study validate the use of Polyherbal formulation for the treatment of asthma.

REFERENCES:

1. Tripathi K D, Essentials of Medical Pharmacology, 5th Edn., Jaypee Brothers Medical Publisher (P) Ltd., New Delhi, **2003**; pp 198-199
2. Rangari VD. Pharmacognosy and Phytochemistry. Vol I, 2nd edi, Career publication, Nashik, **2009**.
3. Pandit P, Singh A, Bafna AR, Kadam PV, Patil J. Evaluation of antiasthmatic activity of *Curculigo orchioides* gaertn rhizomes, Ind. J. Pharma. Sci., **2008**; 20(4): 440-444.
4. Kumar D, Bhujbal SS, Deoda RS, Mudgade SC. *In-vitro* and *In-vivo* Antiasthmatic Studies of *Ailanthus excelsa* Roxb. on Guinea Pigs, J. Sci. Res., **2010b**; 2(1): 196-202.
5. Chandak R, Devdhe S, Changediya V. Evaluation of anti-histaminic activity of aqueous extract of *ripe olives of olea-europea,* J. Pharma. Res., **2009**; 2(3): 416-420.
6. Bhalke RD, Gosavi SA. Anti-Stress and Antiallergic Effect of *Argemone Mexicana* Stems in Asthma, Arch. Pharm. Sci. & Res., **2009**; 1(1): 127-129.
7. Huntley A, Ernst E. Herbal medicines for asthma: a systematic review, Thorax., **2000**; 55: 925-929.
8. Philipson JD. Phytochemistry and pharamacognosy, Phytochemistry, **2007**; 68: 2960–72.
9. Rao SR, Ravishankar GA. Plant cell cultures, chemical factories of secondary metabolites, Biotechnol. Adv., **2002**; 20: 101-53.
10. Kumar V, Parmar NS. Herbs. A potential source for development of new phyto-medicinals, The Pharma Review, **2003**; 1(4): 59-63.
11. Grundmann O, Wahling C, Staiger C, Butterweck V. Anxiolytic effects of a passion flower (*Passiflora incarnata* L.) extract in the elevated plus maze in mice, Pharmazie, **2009**; 64(1): 63-64.
12. Aiyer MN, Namboodiri AN, Kolammal M. Pharmacognosy of Ayurvedic drugs, Pharmacognosy unit. Ayurveda College, Trivandrum, 1957. Al-shaibani IRM, Phulan MS, Arijo A, Qureshi TA. Oovicidal and larvicidal properties of *adhatoda vasica* (L) Extracts against gastrointestinal nematodes of sheep *in vitro*, Pakistan vet. J., **2008**; 28(2): 79-83.
13. Yelne MB, Dennis TJ, Billore KV, Chaudhari BG. 2005. Database of Medicinal Plants Used in Ayurveda, Vol. VII, Central Council for Research in Ayurveda and Siddha, **2005**; 452-475.
14. Dey AC. Indian Medicinal Plants Used in Ayurvedic Preparations. Bishen Singh, Mahendra Pal Singh, Dehra Dun-248001, **1980**; 202.
15. Kelly HW, Sorknes CA. Asthma. In: Pharmacotherapy- A Pathophysiological Aproch, 6th edi, The McGraw-Hill, **2005**; 504.
16. Palit G, Singh SP, Singh N, Kohil KP, Bhargava KP. An experimental evaluation of antiasthamatic plant drugs from the ancient Ayurvedic medicines, Aspects Appl. Immunol., **1983**; 16: 36-41.
17. Pandit P, Singh A, Bafna AR, Kadam PV, Patil J. Evaluation of antiasthmatic activity of *Curculigo orchioides* gaertn rhizomes, Ind. J. Pharma. Sci., **2008**; 20(4): 440-444.
18. Chung KF, Barnes PJ. Cytokines in asthma, Thorax., **1999**; 54: 825.
19. Lichtenstein LM. Mechanisms of allergic inflammation. Progress in Immunology-III: Edited by TE Mandel *et al*, North Holland Publishing, Amsterdam, **1977**; 430-438.
20. Barr RG, Kurth T, Stampfer MJ, Buring JE, Hennekens CH, Gaziano JM. Aspirin and decreased adult-onset asthma, Am. J. respire. Crit. care med., **2007**; 175: 120-125.
21. Gupta SS. Prospects and perspectives of natural products in medicine, Ind. J. Pharmacol., **1994**; 26: 1-12.

22. Kumar PV, Sivaraj A, Madhumitha G, Saral AM, Kumar BS. In-Vitro Anti-Bacterial Activities of *Picrorhiza Kurroa* Rhizome Extract Using Agarwell Diffusion Method, Int. J. Curr. Pharm. Res., **2010a**; 2(1): 30-33.
23. Spina D. Asthma mediators: Current views, J. Pharm. Pharmacol., **2000**; 52: 125-45.
24. Peden DB. The epidemiology and genetics of asthma risk associated with air pollution, J. Allergy and Clin. Immunol., **2005**; 115: 213-219.
25. Bousquet J, Jeffery P, Busse WW, Johnson M, Vignola AM. Asthma from bronchoconstriction to airways inflammation and remodeling, Am. J. Respir. Crit. Care med., **2000**; 161(5): 1720-1745.
26. Jadhav JH, Balsara JJ, Chandorkar AG. Involvement of histaminergic mechanisms in the cataleptogenic effect of clonidine in the mice, J. Pharm. Pharmacol., **1983**; 35: 671-673.
27. Muley MP, Balsara JJ, Chandorkar AG. Intracere broventricular administration of histamine in conscious mice induces catalepsy, Ind. J. Pharmac., **1979**; 11: 277-281.
28. Dhanalakshmi S, Khaserao SS, Kasture SB. Effect of ethanolic extract of some anti-asthmatic herbs on clonidine and haloperidol-induced catalepsy in mice, Ori. Pharm. Experi. Med., **2004**; 4(2): 95-99.
29. Tripathi RM, Das PK. Studies on Antiasthmatic and antianaphylactic activity of *Albizzia lebbeck*, Ind. J. Pharmacol., **1977**; 9(3): 189-194.
30. Ghazanfari T, Hassan ZM, Ebrahimi M. Immunomodulatory activity of protein isolated from garlic extract on delayed type hypersensitivity, Int. Immunopharmacol., **2002**; 2(11): 1541-1549.
31. Ward C, Pais M, Bish R, Reid D, Feltis B, Johns D, Walters EH. Airway inflammation, basement membrane thickening and bronchial hyperresponsiveness in asthma, Thorax., **2002**; 57: 309-16.
32. Hitchcock M. Stimulation of the antigen-induced contraction of guinea pig trachea and immunological release of histamine and SRS-A from sensitized guinea pig lung by 2-isopropyl-3-indoyl.-3 pyridyl ketone L 8027 and indomethacin, Br. J. Pharmacol., **1980**; 71: 65-73.
33. Maity TK, Mandal SC, Saha BP, Pal M. Effect of *Ocimum sanctum* roots extract on swimming performance in mice, Phytother. Res., **2000**; 14(2): 120-121.
34. Murray JF, Nadel JA. Textbook of Respiratory Medicine. 5th edi, WB Saunders, Philadelphia., **2000**; 553-595.
35. Kulkarni SK. Hand book of Experimental Pharmacology. 3rd Edn, Vallabh Prakashan, New Delhi, **2004**; 92-95.
36. Rall TW. Drugs used in treatment of Asthma in Goodman and Gilman (Eds). The Pharmacological basis of Therapeutics. 8th edn, Pergamon, New York, **1990**; 618-637.

How to cite this article:

Sidheshwar Sangram Patil et al.,: Preclinical Evaluation of Polyherbal Formulation Consisting various Indigenous Plants for their Antiasthmatic Activity, J. Pharm. Res., 2015; 4(8): 284-289.

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil