INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD)
© 2026 IJNRD | Volume 11, Issue 1, January 2026 | ISSN: 2456-4184 | IJNRD.ORG

'A SCOPE OF *BILWADI GUTIKA* IN BLOOD EOSINOPHILIA'

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Abstract : *Bilwadi Gutika* is widely used in Ayurvedic Therapeutics to treat various disorders. It is indicated in various poisoning cases like *Sarpa*, *Loota*, *Mooshika*, *Gara* and *Dooshi visha*. It is also used in conditions like Skin Allergies, Skin diseases clinically.

Eosinophils are the WBCs with the normal range 0% to 6%. They are the part of our body's defense system against Allergens and help to protect our body from Fungal and Parasitic infections.[1]

Eosinophilia is a condition characterized by raised count of Eosinophils in the blood or tissue hence two types namely- Blood Eosinophilia and tissue Eosinophilia. Blood Eosinophilia is characterized by raised count of Eosinophills.[2] (Total count more than 6% and Absolute Eosinophil count more than 400 cells /micro ltr of blood) in the blood due to any Allergy, Parasitic infestations or infections.

In Ayurvedic clinical Practice, *BILWADI Gutika* is a drug of choice in *Gara* and *Dooshivisha* which is mostly characterized by allergic conditions like Allergic asthma (*Shwasa*) , allergic skin Manifestations(*Twak vikaras*) etc.[3] which are associated with Eosinophilia.

IndexTerms - *Bilwadi gutika*, Total eosinophil count, Absolute eosinophil count, Blood eosinophilia.

INTRODUCTION

Bilwadi Gutika is a well-known Ayurvedic formulation widely used in the treatment of various disorders. It is indicated in different types of poisoning such as *Sarpa Visha* (snake poison), *Loota Visha* (insect poison), *Mooshika Visha* (rodent poison), *Gara Visha*, and *Dooshi Visha*. Clinically, it is also beneficial in conditions like skin allergies and other dermatological disorders.

Eosinophils are a type of white blood cell (WBC) that normally range from 0% to 6% in the blood. They play a crucial role in the body's defense system against allergens and help protect against fungal and parasitic infections.[1]

Eosinophilia refers to an elevated level of eosinophils in the blood or tissues and is classified into two types: *Blood Eosinophilia* and *Tissue Eosinophilia*. Blood Eosinophilia is characterized by an increased eosinophil count, typically more than 6% or an Absolute Eosinophil Count exceeding 400 cells/µL of blood, which may result from allergic reactions, parasitic infestations, or infections.[2]

In Ayurvedic clinical practice, ***Bilwadi Gutika*** is considered the drug of choice for managing *Gara* and *Dooshi Visha*, conditions often associated with allergic manifestations such as *Shwasa* (allergic asthma) and *Twak Vikaras* (allergic skin disorders).[3] These

conditions are frequently correlated with elevated eosinophil levels. Therefore, it becomes important to scientifically evaluate and substantiate the efficacy of *Bilwadi Gutika* in managing eosinophilia, thereby elucidating its therapeutic potential in allergic conditions.

The present study has been designed based on the principles of *Agada Yoga* (Yoga and Prayoga Vijnana) to assess the efficacy of ***Bilwadi Gutika*** on the physiological variation of eosinophilia. This research aims to explore the role of the formulation in *Samprapti Vighatana* (breaking the pathogenesis) of diseases characterized by raised eosinophil counts.

REVIEW OF LITERATURE

Ingredients of *Bilwadi Gutika* [4]

Table. No: 1

Sl No	Drug	Botanical Name	Part used
1	*Bilwa*	*Aegelo marmelos*	Root
2	*Surasa (Tulasi)*	*Ocemum sanctum*	Flower
3	*Karanja*	*Pongaemia pinnata*	Root
4	*Natham (Tagara)*	*Walleraria wellachi*	Fruit
5	*Suravaha (Devadaru)*	*Cedrus deodara*	Exudate of bark
6	*Haritaki*	*Terminalia chebula*	Fruit
7	*Vibheetaki*	*Terminalia bellarica*	Fruit
8	*Amalaki*	*Embilica officinalis*	Fruit
9	*Shunti*	*Zingeber officinalis*	Rhizome
10	*Maricha*	*Piper nigram*	Fruit
11	*Pippali*	*Piper longum*	Fruit
12	*Haridra*	*Curcuma longum*	Rhizome
13	*Daruharidra*	*Berberis aristata*	Rhizome

Bilwadi Gutika is an *Agada* which is mentioned in the context of *visha*. This *Agada* is indicated in all the *visha* conditions. The yoga mentioned in *Ashtanga Hridaya Uttara sthana* 36th chapter is taken for the study.

BILWA

Bilva (*Aegle marmelos*) is extensively described and used in the Vedic literature. *Bilva* is considered as best *sangrahika* and *deepaniya* drug being *vata kaphahara***.** Stem is good for the heart, effective in rheumatoid arthritis and improves secretion of digestive enzymes. Unripe fruits balance *Kapha* and *Vata doshas*. Ripe fruits are difficult to digest and aggravate all three doshas[1]. The study shows that bilva is having anti- oxidant property. The herbal drugs those show anti-oxidant activity are safe for the use in the treatment of various disease because they do not produce toxic effect in the human body[2]. The role of oxidative stress in genesis of neurodegenerative diseases has been widely studied. The high oxygen consumption rate coupled with low antioxidant potential of the brain is the main triggering factor for the enhanced release of free radical. The study shows that that *Aegle marmelos* may be effective in the therapy of various neurodegenerative diseases, which may be due to effective free radical scavenging property of the plant [3].

Analgesic activity

Study shows that the methanol extract of leaves of *Aegle marmelos* at a dose level of 200 and 300 mg/kg and observed significant analgesic activity on acetic acid induced writhing and tail flick test in mice[4]

Anti-inflammatory and Cardio protective effects

The study shows that aqueous extract of *Aegle marmelos* with the help of rat paw oedema model and assured that *A. marmelos* have anti-inflammatory activity. The various extracts of the leaves of Bael were evaluated for anti-inflammatory activity. The cardio protective activity is due to the presence of aurapten as potent compound. The leaf extract of Bael has preventing effects in isoprenaline-induced myocardial infarction in rats. Further studies concluded that Bael can be used as cardiac depressant[5]

TULASI

Tulasi has been used for thousands of years in ayurveda for its diverse healing properties. It is regarded in Ayurveda as a kind of "elixir of life" and believed to promote longevity[6].

Anti-oxidant property

The antioxidant property of the O. Sanctum plant was stained by dot blot assay method. From this result, methanolic extracts showed maximum antioxidant potential than the other extracts.

This dot blot assay confirmed that these plants have the potential antioxidant property[7].

Analgesic activity

The 'rat tail method' was used to find out the analgesic effect. *Tulasi* showed an increase of 20.34 percent from mild dose, 43.80 per cent from moderate dose and of 51.47 per cent from maximum dose. The effect would remain up to 3 hours with all the three doses. The higher concentration of dose showed better efficiency. The results depict that *Tulasi* had a long-lasting analgesic effect so can be effective in chronic pains[8].

Anti-inflammatory activity

Ocimum santum alone and in combination with indomethacin was studied using Carrageenan-induced rat paw edema. Aqueous extract of O. sanctum (200mg/kg or 400mg/kg) was administered alone and in combination with indomethacin (25mg/kg) to separate group of rats and paw volume was measured by plethysmometer and compared with control group. All the test groups showed significant ($P<0.05$) anti-inflammatory effect in Carrageenan-induced rat paw edema. The reduction of edema by O. sanctum was better than that of the standard anti-inflammatory drug[9].

Neuro protective activity

Different extracts of stem, leaf and stem callus was tested for anticonvulsant activity by maximal electroshock model using phenytonin standard. It was observed that ethanol and chloroform extract of stem, leaf, stem callus were effective in preventing tonic convulsion induced by trans corneal electroshock[10].

Cardio protective and Wound healing property.

Prolong administration of fresh *Ocimum sanctum* leaves augments cardiac endogenous anti-oxidants and prevents isoproterenol induced myocardial necrosis in rats. It was observed that *Ocimum sanctum* at a dose 50 mg/kg are found to demonstrate maximum cardio-protective effect. Several studies show that healing property of *Ocimum sanctum*. Wound healing property of cold aqueous extract of *Ocimum sanctum* leaves along with its effect on tumor necrosis factor alpha was assessed using excision model of wound repair in albino rats. After application of *Ocimum sanctum* extract rate of epithelization with an increase in wound contraction was observed[11].

KARANJA

Karanja (*Pongamia pinnatta*) is mentioned among the *kandughna varga* (itching) by Charaka. It is mentioned in *Rigveda* and *atharva veda*. *Karanja* sticks are fore bidden for rituals but described as the best among tooth sticks. It is distributed throughout

India. It is indicated in arshas (piles), grahani (IBS), unmade (insanity) etc. Chemical constituents are karanjin, pongapin, kanjone, pongol, gamatin, glabrin, 3-methoxy pongapin[12].

Analgesic and Anti-inflammatory activity

The ethanol extract of Karanja was investigated for anti-inflammatory and analgesic activity at the doses (p.o.) of 100, 200, and 400 mg/kg body weight. For evaluation of inflammation carrageenan, histamine- and serotonin induced paw edema served as acute models and cotton pellet–induced granuloma served as a chronic model in rats. The data obtained in this study demonstrated that extract of *karanja* might have analgesic and anti-inflammatory activities [13].

Antioxidant and Antimicrobial properties

A study conducted on "Antioxidant, Antimicrobial Properties and Phenolics of different Solvent Extracts from Bark, Leaves andSeeds of *Pongamia pinnata*" shows that the tested parts of *Pongamia pinnata*, in particular the bark, have better potential for the isolation of antioxidant and antimicrobial agents for pharmaceutical uses than the leaves and seeds[14].

TAGARA

(*Valeriana wallichi*) grows at 1000 ft in Himalayan region. Its useful part is root and is indicated in *apasmara* (epilepsy), *anidra* (sleeplessness), *siroruk* (head ache). Main chemical compositions are hydroxy valeranone, acctoxyvaleranone, linarin, isovalerate, didrovaltratum, valerosidatum, valtrate, acevaltrate[15].

Analgesic activity

A study has shown that both weak central and strong peripheral antinociceptive effect of *Valeriana wallichi*. The data suggested that essential oil exerted peripheral antinociceptive effect via inhibition of prostaglandin synthesis and central analgesic action via opioidergic pathway[16].

Anti-oxidant activity

The methanolic extracts of *Valeriana wallichi* was used in study and also screened for the presence of phyto-chemicals viz. alkaloids, flavonoids, tannins, saponins, glycosides, etc. and their effect on 2,2-Diphenyl-1-picryl-hydraxyl radical (DPPH) which was used to determine the free radical scavenging activity. The occurrence of phytochemical compounds in huge quantity is realistically proportional to the antioxidant activity[17].

Anti-inflammatory activity

Valeriana wallichi was found to be having anti-inflammatory property at dose of 40mg/kg and the anti-inflammatory property of *Valeriana wallichi* is increased with increasing dose[18].

DEVADARU

It is distributed in northwest Himalayan region. Major chemical constituents are p-methyl acetophenone, atlantone, sesquiterpenes, deodarin, toxifolin. Its useful part is *kanda sara and is indicated in kasa (cough), swasa (asthma), krimi (worms), kandu(itching), kushta (skin disease), sopha (swelling)*.[19]

Neuroleptic, Anti- oxidant, Anti convulsant properties[20]

Traditionally the heartwood of *Cedrus deodara* plant was used to enhance cerebral function, balance the mind, body connection, nervous system and strengthen the brain. It was reported to possess CNS depressant and neuroleptic activity. C. deodara was also reported to have good antioxidant property. Two processes were involved to identify the antioxidant components of *Cedrus deodara*. Fractionation and purification was done of dried heartwood powder of C. deodara, first defatted with petroleum ether and then extracted with chloroform. The heart wood extracts of *Cedrus deodara* (ALCD) was studied for anxiolytic and anticonvulsant activity by three experimental models namely Elevated plus maze test, Light dark model, locomotor activity by actophotometer and anticonvulsant activity was studied by using Pentylene tetrazole induced convulsion. It shows good result also.

Wound healing property:

The oil has been reported to possess anti-inflammatory and anti-microbial activities. The plant has also shown wound healing properties and is particularly useful in infective wounds[21].

HARITHAKI

Harithaki (*Terminalia chebula*) is one of the important herbs used in folklore medicine, house hold and traditional medicine. Its fruit rind is used in medicine and one of the ingredients in *Triphala*. Chemical constituents are antraquinone glycoside, chebulinic acid, tannic acid. It is indicated in *sotha (swelling), prameha (diabetes), kushta (skin disease), vrana (ulcer)*[22].

Cardio protective activity

Protective effect of *Terminalia chebula* against lysosomal enzyme alterations in isoproterenol induced cardiac damage in rats was studied. Pre treatment with an ethanol extract of *Terminalia chebula* was found to retain near normal activities of lysosomal enzymes in rats given *Terminalia chebula*. In vitro study with various extracts of the fruit rind showed cardio tonic activity in experiments with normal and hypodynamic isolated frog hearts. It increased the force of contraction and cardiac output without altering the heart rate[23].

Anti-oxidant and Neuro protective activity

The scavenging capacity of *Terminalia chebula* for the antioxidant DPPH was the highest of the extracts tested. The results attributed the *T. chebula* extract with the highest oxygen radical absorption capacity (ORAC). In the FRAP assay, the extracts' ferric reducing antioxidant abilities were *T. arjuna, T. chebula and T. bellerica*. The methanol and water extracts of *Terminalia chebula* exhibit neuro- protective activities against H2O2 induced toxicity toward PC12 cells and are potential candidates for the treatment of H2O2induced neurodegenerative disease. The effective neuroprotective activity of the water extract is consequence of its OH and H2O2 scavenging activities, its greatest extraction yield and its total phenolic and tannin content[24].

Wound healing

Studies shows that the herbal paste preparation obtained from *Terminalia chebula* showed significant ($p<0.05$) improvement to stimulate fibroblast function, enhance synthesis of glycos aminoglycan's and deposition of collagen. Thus, it offers a distinct advantage to wound healing[25].

Analgesic and anti-inflammatory effect

The present study concludes that the ethanolic extract of *Terminalia chebula* fruits possesses analgesic and anti- inflammatory activities in mice and rats at the doses of 250 mg/kg and 500 mg/kg and, 300 mg/kg respectively[26].

VIBHITHAKI

Vibhithaki (*Terminalia belerica*) is distributed in plains and lower hills throughout India. It contains fructose, galactose, mannitol, beta sitosterol, gallic acid, chebulic acid, ellagic acid. It is indicated *in jwara (fever), kasa (cough), swasa (asthma)*[27].

Cardio protective, Anti -ulcer properties

The results of the present study indicate that the prior administration of the *Terminalia belerica* extract attenuates isoproterenol-induced MI. The cardio protective effect of the *Terminalia belerica* extract is probably related to its ability to strengthen the myocardial membrane by its membrane-stabilising action. *Terminalia belerica* extract at the dose level of 300 mg/kg was found to be more effective dose. In this study, the cardio protective potential of *Terminalia belerica* extract is evident.The anti-ulcer activity of ethanolic extract of *Terminalia belerica* fruits was investigated in pylorus ligation and ethanol induced ulcer models in wistar rats. The extract (250 mg/kg & 500 mg/kg) showed significant ($P<0.05$) reduction in free acidity and ulcer index in comparison to the control group[28].

Wound healing and anti- oxidant properties activity:

Studies have proved that the paste of *Terminalia belerica* have efficacy on wound healing. Herbal paste preparation of*Terminalia belerica* showed significant improvement on maturation, wound contraction and epithelialization in an experimental study. Crude aqueous extract of the fruits of *Terminalia belerica* have antioxidant properties since these contains enzymatic and non- enzymatic antioxidants, these can be very effective against microbes causing various diseases. In vitro assessment of the antioxidant activity of ethanolic fractions of the plant to scavenge 2, 2- Diphenyl-1-picrylhydrazyl (DPPH) and highly reactive hydroxyl radicals showed that the semi pure compounds present in the fractions are useful potential source of antioxidants[29].

AMALAKI

It can be seen throughout India. The main chemical constituents are Vitamin. C, phyllemblin, linoleic acid, indole acetic acid, corilagin, ellagic acid and phyllembic acid. It is indicated *in prameha (diabetes mellitus), raktha pitta (bleeding disorder), netra roga (eye disease), kushta (skin disease) arsha (piles),* etc[30].

Anti-inflammatory and analgesic activity

The anti-inflammatory and analgesic activities of the standardized water extract from the fruit of *Emblica officianalis* prepared according to the THP seem to be similar to NSAIDs rather than to steroidal drugs. Inhibitory effect on the synthesis and/or release of inflammatory or pain mediators may be the main mechanisms of action of P. emblica[31].

Antioxidant activity

Vitamin C, tannins and flavonoids present in amla have very powerful anti-oxidant activities, this help in elevation of hepatic anti-oxidant system and lowering of cytotoxic products[32].

Cardio- protective activity

Emblica officinalis fruit juice may be beneficial for the treatment of myocardial damage associated with type 1 diabetes mellitus. The activity of *Emblica officinalis* fruit juice can be attributed to the concentration of the polyphenol present. Results demonstrate the cardio protective potential of E. officinalis attributed to its potent antioxidant and free radical scavenging activity as evidenced by favorable improvement in hemodynamic, contractile function as well as tissue antioxidant status[33].

Anti-ulcer Activities

Methanolic extract of *Emblica officinalis* was studied against ulcer. *Emblica officinalis* had significant ulcer protective and healing effects and this might be due to its effects both on offensive and defensive mucosal factors[34].

Neuro protective activity

EO extract may be able to suppress oxidative stress of neuronal cells within the brain possibly indicating its neurotonic effects. EO seems to have a therapeutic potency possibly as alternative therapy for preventing or delaying progression of neurodegenerative diseases[35].

SUNTHI

Sunthi (*Zingiber officianale*) is distributed throughout India. It is indicated in *sula (pain), amavata (rheumatoid arthritis), adhmana (distension of abdomen), athisara (diarrhoea), shlipada (filariasis), kasa (cough), swasa (asthma), hrudroga (heart disease), sopha (inflammation), arshas (piles), hikka (hiccough)*, etc[36].

Anti-oxidant activity

A study has proved that ginger extract is good source of polyphenolic compounds, including gingerols, shogaols, paradolsand gingerdions. It manifested a very good scavenging of ABTS radical cation and DPPH radical, respectively[37].

Anti-inflammatory, Analgesic activity

The rhizome extract of *Zingiber officianale* was investigated for anti-inflammatory and analgesic property in albino rats and mice respectively. The extract (50 and 100 mg/kg) produced significant inhibition of carrageenan induced rat paw oedema and reduction in the number of writhing induced by acetic acid in mice. The result shows that rhizome extract of *Zingiber officianale* possess anti-inflammatory and analgesic effect[38].

Cardio vascular effect

In vitro research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardio tonic properties at higher doses. Both shogaol and gingerol, and the gingerdiones, are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis[39].

Neuro proctective effect

Study have shown that *Z. officinale* is a neuro protectant. Dose-dependently enhances the memory with improvement in the locomotor and muscle grip strength in 3-NP-administered rats[40].

PIPPALI

It is found in hot parts of India. The chemical constituents are essential oil, sequiterpenes, caryopyllene, pipenonaline, pipercide, sesamin, beta sitosterol, piperine, 4, 5 dioxoaporphines. It is indicated in *udara (ascites), pliharoga (spleenomegaly), jwara (fever), kushta, (skin disease) prameha (diabetes),* etc [41].

Analgesic activity

Piper longum root has shown significant result as an opioid type analgesic in rat tail flick method and as a NSAID type analgesia using acetic acid writhing method. An aqueous suspension of *Piper longum* root powder given orally to mice and rat in doses of 200, 400, 800 mg/ kg. The delay in reaction time for thermal stimulus in rat and number of writhing to chemical stimulus in mice was detected in each group. The 400 and 800 mg/kg showed 50%protection against writhing[42].

Anti-oxidant and anti-microbial properties

Study shows that the chloroform extract of *Piper longum* displayed the most effective in vitro antibacterial activity tested against *Micobacterium smegmatis* indicating their potential as a source of anti-mycobacterial drugs. Also, the chloroform extract exhibited greater amount of phenolic and had significant antioxidant activity compared to the hexane, ethyl acetate, ethanol, hydro ethanol and aqueous extracts. This validates the correlation of the total phenolic content of plant extracts with their antioxidant and antimicrobial properties[43].

Anti-inflammatory and Antiulcer activity

The fruit extract of *Piper longum* were reported to possess anti-inflammatory activity in carrageanan rat paw edema. And the piper extract and piperine possess inhibitory activities on prostaglandin and leukotrienes Cox-1 inhibitory effect and thus exhibit anti-inflammatory activity. The antiulcer activity was demonstrated by water decoction of ginger making up one of the constituents of *Mahakasyaya* drugs along with water decoction of *P. longum* and colloidal solution of *Ferula asafoetida* has been reported to protect against CRS, ASP and PL- induced gastric ulcers in rats. Piperine, an alkaloid of long peppers, inhibited gastric emptying (GE) of solids/liquids in rats and gastrointestinal transit (GT) in mice in a dose and time dependent manner. GE inhibitory activity of piperine is independent of gastric acid and pepsin secretion[44].

Cardio protective activity

Guineensine, isolated from chloroform extract inhibited ACAT activity in a dose dependent manner. An amide namely dehydropipernonaline having coronary vaso-relaxant activity was isolated from the fruit of *Piper longum*[45].

Neuro protective activity

PIP presented a neuro protective action, probably a consequence of its anti-inflammatory and antioxidant properties, making the drug a potential candidate for the treatment of neurodegenerative diseases[46].

MARICHA

Maricha can be found in hills of South western India. The main chemical constituents are piperene, piperethine, citronellol, cryptone, piperonal, camphene, beta alanine, carotene, ascorbic acid, pipercide[47].

Anti-oxidant, Analgesic and Anti -inflammatory activity

In vitro studies revealed that Piperine inhibited free radicals and reactive oxygen species, therefore known to possess protective effects against oxidative damage. The analgesic activities of both piperine and morphine in the tail flick assay were reversed on pre-treatment of animals with naloxone at dose of 5 mg/kg (i.p.). These results revealed the analgesic activity of piperine which possibly mediated via opioid pathway**.** The piperine was evaluated for the anti-inflammatory, analgesic, and anti-arthritic activities. The in vitro anti-inflammatory activities were evaluated on interleukin 1β stimulated fibroblast like synoviocytes obtained from rheumatoid arthritis[48].

HARIDRA

It contains curcumene, curcumenone, curcone, curdione, cineole, curzerenone, eugenol, camphene, camphor, borneol, curcumins. It is indicated in *prameha, kushta, krimi, kandu, vrana, pandu*[49].

Anti-inflammatory activity

Research study has shown curcumin to be a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation[50].

Analgesic activity

Different extracts of Curcuma longa at three doses 100, 200 and 400 mg/kg were evaluated for their analgesic activity using different animal models of analgesia. Shows significant analgesic activity in the tail flick test at 400 mg/kg one hour after administration[51].

Antioxidant activity

Curcuma longa exhibited highest antioxidant activity 74.61%. This activity could be attributed to both phenol and curcumin content. Moderate antioxidant activity is possible due to 95% oil content having major constituents, camphor, methyleugenol, pentadecanoic acid[52].

Cardio protective

Oral administration of Curcuma longa ethanolic or water extract (200 mg/kg) prior to doxorubicin produced a significant protection which was evidenced by significant reduction in mortality. Curcuma longa extracts renders resiliency against doxorubicin cardio toxicity due to their contents of poly phenolic compounds[53].

Neuro protective activity

Curcumin and manganese complex of curcumin are protective against vascular dementia[54].

DARUHARIDRA

It is mainly indicated in *prameha (Diabetes mellitus), kushta (skin disease), netra roga (eye disease), kamala (jaundice)* [55].

Anti-inflammatory activity

The ethanolic and aqueous extracts of *Berberis aristata* DC. Heartwood exhibited significant anti-inflammatory activity with percent inhibition 33.40% & 44.50% at a dose of 25 mg/kg, p.o. and 52.20% & 57.0% at a dose of 50 mg/kg, p.o., respectively. Whereas standard drug, Indomethacin showed an inhibition of 64.80%[56].

Anti-oxidant activity

The antioxidant activity of the methanolic extract were determined by DPPH (1, 1-Diphenyl-2-picryl hydrazyl) assay and Nitric oxide scavenging method[57].

BLOOD EOSINOPHILIA

Eosinophils are a kind of blood granulocytes that express cytoplasmic granules that contain basic proteins and bind with acidic dyes like “eosin.” They derive from bone marrow, and IL-5, IL-3, and GM-CSF stimulate their production. They have a circulating half-life of 4.5 to 8 hours. They can reside in tissues, mostly in the respiratory tract and gastrointestinal tract, for 8 to 12 days. Eosinophils are less than 5% of circulating leukocytes. Eosinophilia is defined as an increase of circulating eosinophils >500 /mm^3.[19]

Based on the counts, eosinophilia can subdivide into different categories: mild (500 and 1500/mm^3), moderate (1500 to 5000/mm3), and severe (> 5000/mm^3). Hypereosinophilic syndrome is defined as an absolute eosinophil count greater than 1500/mm3 on two occasions at least one month apart or marked tissue eosinophilia.[20]

ETIOLOGY

Eosinophilia can be primary or secondary[21]:

Primary causes [22]:

- Chronic eosinophilic leukemia
- Myeloid and lymphoid neoplasms with *rearrangements of PDGFRA, PDGFRAB, or FGFR1* genes

- Hereditary eosinophilia
- Idiopathic hypereosinophilic syndrome

Secondary causes[22]:

- Parasitic infestations: ancylostomiasis, ascariasis, cysticercosis, echinococcosis (hydatid cyst), schistosomiasis, strongyloidiasis, trichinellosis, visceral larva migrans (toxocariasis)
- Fungal and bacterial infections: bronchopulmonary aspergillosis, chronic tuberculosis (occasionally), coccidioidomycosis, disseminated histoplasmosis, scarlet fever
- Allergic disorders: bronchial asthma, hay fever, Stevens-Johnson syndrome, drug, and food allergic reactions, DRESS syndrome
- Skin diseases: Atopic dermatitis, eczema, pemphigus, *Mycosis fungoides*, Sezary syndrome
- Graft versus host reaction
- Connective tissue disease: Chrug-Strauss syndrome, eosinophilic myalgia syndrome
- Miscellaneous: reactive pulmonary eosinophilia, tropical eosinophilia, pancreatitis, eosinophilic gastroenteritis

EPIDEMIOLOGY

The incidence and prevalence of eosinophilia are not well described. There is no sex predilection for eosinophilia. However, there can be geographical influences depending on its cause. Parasitic infestations are more prevalent in tropical countries. Allergic disorders are commonplace in developed countries.[23] Idiopathic hypereosinophilia is diagnosed between 20 and 50 years of age, but extreme ages at both ends of the curve are also known to occur.

PATHOPHYSIOLOGY

Eosinophils become differentiated in bone marrow, and once they leave the marrow, they stop maturing further. They reside in tissues, mostly outside the vasculature. In eosinophil related disorders, eosinophils are recruited into the involved tissues. T helper-2 cells mediated immune responses, and IL-5 production induce eosinophilopoiesis and eosinophil activation. The major cytokine responsible for eosinophil production and activation is IL-5 [9,10]. After activation, eosinophils degranulate and release the cationic proteins into the tissues through which eosinophils perform their functions. These released proteins can be proteolytic enzymes, which can cause damage to the host wall as well. Eosinophil also releases cytokines, like IL-10 and IL-14, which aid in maintaining homeostasis and immunoregulation.[24,25]

HISTOPATHOLOGY

An eosinophil is around 12 to 17 µm in diameter and has a segmented nucleus. It has abundant cytoplasmic granules that contain proteolytic enzymes. Four major proteins comprise the granules: major basic protein (MBP1), eosinophilic cationic protein (ECP), eosinophil derived neurotoxin (EDN), and eosinophil peroxidase (EOP). They stain red-orange with Romanowsky stains.

HISTORY AND PHYSICAL

Due to the heterogeneous manifestations of the disease and severity varying from mild to end-organ damage, comprehensive history taking and diligent physical examination is extremely important, and sometimes enough, for diagnosis. Skin, pulmonary, and gastrointestinal organ systems are commonly involved. Constitutional symptoms like low-grade fevers, night sweats, fatigue, weight

loss can occur in multiple conditions, including myeloproliferative and lymphoid neoplasms, Churg Strauss syndrome, DRESS syndrome.

Skin rashes, pruritus can be seen in cutaneous T cell lymphoma, eczema. Dyspnea, cough, wheezing can be seen in multiple conditions, including bronchopulmonary aspergillosis, Loeffler's syndrome, hay fever, asthma, reactive pulmonary eosinophilia, Churg strass syndrome. Detailed travel history, work environment, drug history, close contacts with HIV, syphilis helps identify infections, parasitic infestations, and drug adverse reactions.[26,27] Physical examination should be complete, including a skin assessment, lung auscultation to look for rhonchi, wheezes, abdomen exam to look for splenomegaly.

EVALUATION

Secondary causes of eosinophilia should be ruled out first. The evaluation for primary eosinophilia should begin with screening peripheral blood for FIP1L1- PDGFRA gene fusion. Diagnostic testing should start with peripheral smear. Cytogenetic testing and FISH analysis can be performed on peripheral blood as well.

Concurrent cytophilias or cytopenias, if present, can help with diagnosis. In that case, a bone marrow biopsy, along with karyotype and genetic screen of chromosomes, may be required.[28]

B12 level and tryptase level, along with cytogenetic/immunophenotypic testing and marrow findings, help diagnose chronic mastocytosis, acute/chronic myeloid leukemia, myelodysplastic syndrome, and MDS/MPN overlap. When skin rashes are present, skin biopsy helps to diagnose cutaneous disorders like pemphigoid, eczema, mycosis fungoides, and Sezary syndrome. Imaging of the chest helps diagnose aspergillosis, Loeffler syndrome, and Churg Strauss syndrome. Ultrasound abdomen helps to evaluate for splenomegaly. Stool testing helps to assess for parasitic infections.

MANAGEMENT

Management depends on the underlying cause. The goal of the therapy is to mitigate end-organ damage from eosinophilia.[28] In mild cases without any symptoms or signs of organ involvement, a conservative approach can be undertaken. In emergency conditions with hemodynamic instability or organ failure, treatment with IV steroids is important.[26]

For some conditions like drug and food allergies or infections, treatment can be simple, like withdrawing the offending agent or treating it with antibiotics. But in some conditions, due to the varying clinical manifestations and multi-systemic involvement, an interprofessional approach involving hematologists, pulmonologists, and infectious disease specialists, might be necessary. In steroid-resistant cases of hypereosinophilic syndrome and chronic eosinophilic leukemia, hydroxyurea and interferon-alpha have demonstrated efficacy.

In aggressive forms of the disease, second-line cytotoxic agents and stem cell transplants have proven some benefits. Antibody use against interleukin-5 (IL-5) (mepolizumab), the IL-5 receptor (benralizumab), and CD52 (alemtuzumab), as well as other targets on eosinophils, continues to be an active area of investigation.[27,28] Timely intervention is vital to reduce morbidity and mortality.

DIFFERENTIAL DIAGNOSIS

Diagnoses can be narrowed down based on the predominant system involved. For example, when manifested with pulmonary symptoms: asthma, bronchopulmonary aspergillosis, with hay fever: skin involvement: *Mycosis fungoides*, Sezary syndrome, eczema, and bullous pemphigoid.

PROGNOSIS

Prognosis can be varying from mild disease to fatal outcome, depending on multiple factors like the cause of the eosinophilia, the presence of organ damage, the subtype of eosinophilia, and the timeline of intervention.

ALLERGY[29,30]

DERIVATION

The word allergy is derived from Greek words “allos” which means “altered” and “ergos” which means energy.

DEFINITION

When an individual has been sensitized to an antigen, further contact with that antigen can cause tissue damaging reactions is called Allergy.

TYPES

There are four types of Hypersensitivity reactions,

1)Type1 Hyper sensitivity reaction or Immediate Hypersensitivity reaction

2) Type2 Hyper sensitivity reaction or Cytotoxic reaction

3) Type3 Hyper sensitivity reaction or immune complex mediated reaction

4) Type4 Hyper sensitivity reaction or cell mediated or Delayed hypersensitivity reaction.

Type1 Hyper sensitivity reaction or Immediate Hypersensitivity reaction

This is of two types

a)Anaphylaxis

b)Atopic or Allergic Reaction

Anaphylaxis

The antigen reacts with Specific class of antibody,reaginic antibodies(IgE),bound to the surface of mast cells and basophils.Interaction of antigen with IgE antibodies causes degranulation of mast cells and basophils with massive liberation of histamine and other mediators of immediate hyper response,leading to Anaphylaxis.mediators released from mast cells and basophils are :

Those that increase vascular permeability and contract smooth muscles.eg,histamine,PAF,SRS-A,bradykinin.

Those that are chemotactic or activate other pro-inflammatory cells.eg,leukotrine B4,eosinophil and neutrophil chemotactic factor.

Those that modulate the release of other mediators.eg,bradykinin,PAF,Prostaglandin.

Those which cause termination of inflammatory response.

Under physiological conditions,mast cell triggering forms avital part of the acute inflammatory defense reaction.

ALLERGIC REACTION

Allergens like Pollen,animal dander,house dust mites and certain food stuffs which when enters into the body binds with cell bound IgE antibody in the bronchial tree,nasal mucosa or the skin, releases mediators giving rise to localized reactions such as Asthma,Rhinitis or Urticaria.

Allergen

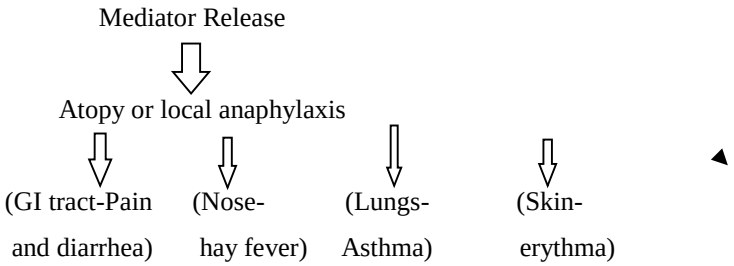
⇩

IgE synthesis

⇩

Mast cell Degranulation

⇩



Type1 Hypersensitivity reaction occurs in subject of atopic allergy.Though atopic allergies run in families,studies with individual populations suggest that there is a close assosciation of high level of IgE in the serum and incidence of atopic diseases.It has also been shown that IL-4 derived from TH2 cells is involved in isotypes switch to IgE and that have genetic predisposition.

This reaction is mediated by IgE antibody fixed on cell surface possessing Fc receptors.On binding with the antigen,the IgE bound tissue mastcells or the release of vaso active amines such as histamine,leading to complex phenomenon at the site of contact of antigen involving contraction of smooth muscles and dialatation of capillaries with outpouring of vascular content and tissue fluid to cause anaphylaxis.Continuation of an acute episode to a chronic stage is attributed to the recruitment of tissue damaging eosinophils through IL-5 derived from mast cells,eosinophils,primed TH2 cells.Otherwise anaphylaxis clinically manifest as mild irritatation to severe anaphylactic shock such as hay fever,bronchial asthma and penicillin allergy.

Immediate hypersensitivity reactions are seen with in 12 hours ie the antigen challenge is initiated by basophil mediated reactions(Type 1)and by performed antibodies(Type 1&Type 2)

Diagnosis

Prick test

Provocation test

Radio-allergosorbant test

Treatment for Type1 Hyper sensitivity reaction

Allergy can symptomatically be treated by the use of antihistamines and long acting beta-antagonist and leukotriene antagonists sodium chromoglycate to stabilize mast cells and inhibit broncho constriction and theophylline conventionally used as bronchodialators in asthma.Theophilline also inhibit IL-5 effect on eosinophils.Desensitization can be donewith a course of antigen in order to produce blocking IgG antibodies.

CALCULATION OF ABSOLUTE EOSINOPHILIC COUNT [31]

Eosinophil diluting solution-Dunger's solution

Stock Solution-

Eosin yellow-0.5gm

Formaldehyde(40%)-0.5 ml

Phenol (95% aqueous)-0.5 ml

Distilled water up to 5 ml

Procedure-suck blood up to 0.5 markin a wbc pippetteand dilute up to 11 mark with diluting fluid.Gently rotate the pipette.Discard first 3 or 4 drops of fluid.Charge Neubauer counting chamber and allow it to stand for 3 minutes, so that the cells settles down.

Count all the Eosinophils in the whole of rulede area.

Calculation-AEC=N x $\frac{1}{}$ x dilution

Vol

N=Number of cells in the ruled area

Vol=length x breadth x depth

=3x3x0.1

=0.9

=N x 1 x20

0.9

=N x10 x 20

9

=N x 200

9

=N x22.2

Normal value=40-440 cells / cu m

Preparation of *Bilwadi Gutika*

The steps included in the preparation of ***Bilwadi Gutika*** are-

- Collection of Drug
- Preparation of *Choorna*
- *Bhavana*
- Rolling of tablets

Collection of Drugs

The drugs are collected from

Alva Pharmacy, Mijar.

Preparation of *Choorna*

The drugs mentioned in the *yoga* are cleaned and dried properly.They are finely powdered and sieved.If there are a number of *drugs* in the *yoga*,the drugs are separately powdered and sieved.Each one of them is weighed seperartely and then mixing them together is preferred.[1]

Bhavana and rolling of tablets

Choorna is taken in a *Khalva yantra* and quantity sufficient *Aja mutra* is poured over the *Choorna*.Then it is pounded till the *Aja mutra* is completely absorbed by the *choorna*. This process is repeated for several times by adding sufficient amount of *Aja mutra*. When it attains a semi-solid mass,roll it into pills and dry it in sun shade.The tablet prepared so is highly potent,as it posess the quality of *Aja Mutra* also.[2]

Table. no: 2 **Ingredients and quantity of *Bilwadi gutika***

DRUGS	***CHOORNA***	**TABLETS**
Bilwa	310 gms	6000 Tablets of 500 mg is prepared from 3500 gms of *choorna* after *Bhavana* with *Aja mootra.*
Surasa	310 gms	
Karanja	310 gms	
Tagara	310 gms	
Devadaru	310 gms	
Haritaki	310 gms	
Vibheetaki	310 gms	
Amalaki	310 gms	

Shunti	310 gms	
Maricha	310 gms	
Pippali	310 gms	
Haridra	310 gms	
Daruharidra	310 gms	

PHARMACEUTICAL ANALYSIS OF BILWADI GUTIKA

QUALITATIVE TEST	
COLOR	YELLOWISH GREEN
ODOUR	CHARACTERISTIC
TASTE	ASTRINGENT , PUNGENT

Table. No: 4

QUANTITATIVE TEST	**FOUND**	**LIMIT**
TABLET HARDNESS TEST	3kg/cm^2	3 – 5 kg/cm^2
FRIABILITY	0.30%	< 1%
UNIFORMITY OF WEIGHT	1%	< OR= 1%
DISINTEGRATION TIME	7MIN 50SEC	30 MINS
LOSS ON DRYING	6.47%	< 10%
DISSOLUTION	95%	> 75 %

5.7 B Pharmaceutical evaluation of Tablet[3]

1. Determination of Ph[4]

- The pH meter was calibrated with standard buffer solutions of pH 4.0 and 9.2 at 30 °C.
- The electrode was rinsed with distilled water and dried with filter paper before each reading.
- A 10% w/v solution of tablet (1 g in 10 mL distilled water) was prepared.
- The electrode was immersed in the solution, and the pH was recorded.

2. Loss on Drying (LOD) at 105 °C[5]

- About 1 g of sample was weighed in a clean, dry silica crucible.
- The crucible with sample was weighed and then placed in a hot air oven at 105 °C until constant weight was achieved.
- The crucible was reweighed, and the loss in weight was calculated.

3. Hardness Test[6]

- The hardness of tablets was determined using the Monsanto hardness tester.
- Each tablet was placed between the fixed and movable jaws of the instrument.

- Pressure was gradually applied by turning the screw knob until the tablet broke.
- The force required to break the tablet was noted in kg/cm².

4. Uniformity of Weight

- Twenty tablets were randomly selected and weighed individually.
- The average weight was calculated, and each tablet weight was compared with the mean value to assess uniformity.

5. Friability[7]

- Tablets were weighed and placed in a friability test apparatus.
- The chamber was rotated at 25 rpm for 4 minutes (100 revolutions).
- Tablets were then reweighed, and the percentage weight loss was calculated.

6. Disintegration Test

- The test was performed using a standard disintegration test apparatus.
- One tablet was placed in each tube, along with a disc.
- The apparatus was suspended in a beaker containing water at 37 °C.
- The time taken for complete disintegration of all tablets was recorded.

7. Dissolution Test

- Dissolution studies were performed in acidic media (pH 1.2, 1.5, 2.0, 2.5).
- The medium was maintained at 37 °C, and the apparatus was operated at 100 rpm.
- Tablets were placed in the basket, and dissolution was observed until homogenous mixture formation.

8. Microbial Contamination Test[8]

- Nutrient agar medium was prepared and sterilized in petri dishes.
- The sample solution was prepared in sterile distilled water and streaked onto the medium.
- Plates were incubated at 36 °C for 24 - 48 hours.
- Growth was observed to check microbial contamination.

I. DISCUSSION ON MODE OF ACTION OF *BILWADI GUTIKA* ON BLOOD EOSINOPHILIA

SN	Drug Name	Rasa	Guna	Virya	Vipaka	Karma
1.	Bilwa	Kashaya, Tikta	Laghu Ruksha	Ushna	Katu	Kapha-Vataghna, Vishamjwaraghna, Shothaghna, Balya, Raktasthambhak, Grahi, Hrudya.
2.	Karanja	Katu, Kashaya, Tikta	Laghu Ruksha	Ushna	Katu	Kapha-Vata Shamaka, Krimighna, Janthughna, Raktashodhak, Kustaghna, Vishaghna, Shothaghna, Vedna Sthapana, Deepana, Pachana.
3.	Surasa	Katu, Tikta	Laghu, Ruksha	Ushna	Katu	Kapha-Vataghna, Vishaghna, Krimighna, Vishamjvaraghna, Deepana Pachana, Anulomana, Janthughna, Shothaghna, Hrudya, Shwasakasahikka-Parshwashoolhara.
4.	Natam	Tikta. Katu Kashaya	Laghu Snigdha	Ushna	Katu	Kapha-Vatashamaka, Vishaghna,Vednasthapaka, Jwaraghna, Bootaghna, Madahara,Shirorogahara, Akshepahara, Saraka, Medhya.
5.	Surawha	Tikta	Laghu, Snigdha	Ushna	Katu	Kapha-Vata Shamaka, Deepana, Kasashwasahikkahara, Shothahara, Kandughna, Jwaraghna, Tandrahara, Kushtaghna Bhootaghna, Krimighna, Raktaprasadana.
6.	Haritaki	Panchrasa Lavan Varjit	Laghu Ruksha	Ushna	Madhura	Tridoshahara, Anulomana, Rasayana, Hrudya, Indriya Prasadana, Medhya, Shothahara, Vednasthapana, Vrushya Krimighna, Kasashwasapliha-Rogahara, Vishamjwarahara.
7.	Bibhitaki	Kashaya	Laghu, Ruksha	Ushna	Madhura	Tridoshahara, Krimighna, Shothhara, Raktasthambhana, Vednasthapana, Deepana, Anulomana, Jvaraghna, Shwasakasavamigara-Nashna.
8.	Amalaki	Amla Pradhan Lavana Varjit	Guru Ruksha	Sheeta	Madhura	Tridoshahara, Rasayana, Hrudya, Vyasthapana, Kanthya, Jwaraghna, Kasahara, Raktapittaghna, Shulaprashmana, Dahaprashmana, Deepana, Anulomana.
9.	Shunti	Katu	Laghu, Snigdha	Ushna	Madhura	Vata-Kaphahara, Deepana, Shothahara, Shoolaprashmana, Hrudaya, Atisarakasashwasa-Hikkahara,

						Vednasthapana, Naadi Utejaka. Jwarahara
10.	*Maricha*	*Katu*	*Laghu, Tikshna*	*Ushna*	*Katu*	*Vata-Kaphahara, Krimighna, Vishaghna, Bhootaghna Hrudya, Kasashwasahara, Deepana, Pachana, Shoolaprashmana.*
11.	*Pippali*	*Katu*	*Laghu, Snigdha, Tikshna*	*Ushna*	*Madhura*	*Kapha-Vata Shamaka, Kushtaghna, Balya Jwaraghna, Rasayana, Hrudya, Deepana Shoolaprashmana, Janthughna Hikkanigrahana, Pachana, Shwaskasa-Pliharogahara.*
12.	*Haridra*	*Tikta Katu*	*Ruksha Laghu*	*Ushna*	*Katu*	*Kapha-Vata Shamaka, Kushtaghna, Jwaraghnavishaghna, Krimighna, Raktadoshahara, Pitta Rechaka, Shothahara, Vednasthapana.*
13.	*Daru-haridra*	*Tikta, Kashaya*	*Ruksha Laghu*	*Ushna*	*Katu*	*Kapha-Pitta Shamaka, Katu-Paushtika Netrya, Vishaghna, Varnya, Shothahara, Vednasthapana, Kandughna, Krimighna, Raktashodhaka, Vishamjvaraghna*
14.	*Basta Mutra*	*Katu, Lavan*	*Laghu, Ruksha, Tikshna*	*Ushna*	*Katu*	*Kaphaghna, Vatakara, Kasashwasaghna, Shophaghna.*

II.

Karma	*Bilwadi Gutika*
Deepana	*Surasa, Trikatu, Surahva, Triphala*
Pachana	*Triphala, Trikatu,*
Grahi	*Trikatu, Aja-Mootra.*
Anulomana	*Tripahala*
Krimighna	*Surasa, Karanja, Surahva, Pippali, Maricha, Haridra, Aja-Mootra,*
Vishaghna / Garanashana	*Surasa, Karanja, Nata, Bibhitaki, Haridra*
Jwaraghna	*Surahva, Haritaki, Amalaki, Shunti, Pippali.*
Janthughna / Bhootaghna	*Surasa, Karanja, Nata, Devdaru, Maricha,Pippali*

III.

IV. Blood eosinophilia is a hallmark feature in various allergic disorders such as asthma, allergic rhinitis, atopic dermatitis, and eosinophilic esophagitis. In these conditions, eosinophils are recruited to sites of inflammation in response to allergens or other triggers. Once activated, eosinophils release inflammatory mediators such as **histamine, prostaglandins, leukotrienes, cytokines,**

and reactive oxygen species (ROS), which contribute to tissue inflammation, edema, and hypersensitivity reactions. Persistent eosinophilic activation can result in tissue damage, fibrosis, and chronic inflammation.

V. The therapeutic approach to allergic eosinophilia involves controlling inflammation, reducing immune hyper-responsiveness, scavenging free radicals, and improving metabolic balance. *Bilwadi Agada*, with its unique combination of herbs and substances, offers potential benefits across these domains, as outlined below:

VI.

VII. *Bilwadi Agada* comprises ingredients primarily possessing *katu*(pungent), *tikta* (bitter), and kashaya(astringent) tastes. These properties contribute to its therapeutic effects. Nearly all the components of the formulation possess *dipana* (digestive), *pachana(carminative), and jwarahara* (antipyretic) properties. The formulation aims to restore the proper functioning of *agni* (digestive fire) in order to facilitate optimal metabolism and facilitate healing at the site of the sting. The analysis of the properties of *Bilwadi Agada* reveals that 85.71% of the constituents possess the *ushna* (warm) virya, with 68.28% exhibiting *vataghna*(alleviating *vata*) properties, and 78.57% displaying *kaphaghna* (balancing *kapha*) effects. This distribution suggests that *Bilwadi Agada* has the potential to provide relief from various types of pain and swelling resulting from insect bites[1]. *Bilwadi Agada* is believed to exert its effects through inhibiting the synthesis of prostaglandins and exhibits potential anti-inflammatory properties. It may also suppress the activity of CYP450 enzymes, which play a crucial role in the production of toxic metabolites such as NAPQI [2]. The root of *A. marmelos* (*bilva*) exhibited significant acute anti-inflammatory activity, which was attributed to the inhibition of mediator release, including histamine, serotonin, and prostaglandins. This effect is believed to be mediated by the presence of chemical constituents such as marmin, lupeol, and others [3]. It is speculated that the fixed oil derived from O. sanctum (holy basil) has the potential to inhibit both the cyclooxygenase and lipoxygenase pathways involved in arachidonic acid metabolism. This dual inhibitory property may be complemented by the antihistaminic effects of the fixed oil[4]. Karanjin and pongamol, which are exclusive furano-flavonoids found in the seeds of karanja, have demonstrated anti-inflammatory properties in previous animal models. These unique compounds exhibit potential as agents with anti-inflammatory effects [5]. *Cyperus rotundus (musta)* may act by inhibiting the production or release of pro-inflammatory mediators such as cytokines, chemokines, and prostaglandins. These mediators are involved in the inflammatory response and can contribute to skin inflammation [6]. *Triphala* exhibits dual effects of anti-inflammatory and antinociceptive activities. The anti-inflammatory effect is likely achieved through the inhibition of the cyclooxygenase pathway without exerting steroidal-like action. On the other hand, the antinociceptive activity of the *Triphala* may involve both peripheral and partial central mechanisms [7]. The efficacy of Goat Urine as antioxidants can be attributed to their ability to scavenge superoxide anions, inhibit nitrite formation, remove hydroxyl radicals, and exhibit reducing ability. This robust antioxidant activity could be attributed to the presence of volatile fatty acids identified through GC-MS analysis in an invitro study. The inhibition of edema by Goat's urine may be attributed to the suppression of histamine H1 receptor and histidine decarboxylase gene transcriptions. Moreover, the mechanism could also include the inhibition of inflammatory enzymes (iNOS and COX-2) and their products (NO and PGE2) [8]. Likewise, each of the constituent drugs in *Bilwadi Agada* contributes to its multifaceted properties, including anti-inflammatory, antioxidant, immunomodulatory, and detoxifying effects.

CONCLUSION:

Bilwadi Agada, through its predominantly *katu*, *tikta*, and *kashaya rasa* profile with *ushna virya* and *kapha–vata shamaka* properties, demonstrates a rational Ayurvedic formulation for conditions associated with inflammation, toxicity, and immune dysregulation. The collective actions of its ingredients—*deepana*, *pachana*, *jwaraghna*, *krimighna*, *vishaghna*, and *shothahara*—support restoration of *agni*, correction of *ama*, and mitigation of inflammatory responses. From a contemporary perspective, the formulation exhibits anti-inflammatory, antihistaminic, antioxidant, and immunomodulatory activities through inhibition of prostaglandins, cytokines, histamine pathways, and oxidative stress. These mechanisms are particularly relevant in allergic disorders characterized by eosinophilia, where persistent inflammation and hypersensitivity predominate. Thus, Bilwadi Agada emerges as a holistic therapeutic option with potential benefits in managing allergic eosinophilia and related inflammatory conditions by integrating classical Ayurvedic principles with experimentally supported pharmacological actions.

To support this review of literature the clinical study has been registered under Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

CTRI REG NO :- REF/2025/06/107739

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