



Review Article

A CRITICAL ANALYSIS OF *BALCHATURBHADRA CHURNA* IN MANAGEMENT OF CHILDHOOD DISORDERS- EVIDENCES FROM AYURVEDA

Nitu Sinha^{1*}, Nisha Kumari Ojha²

^{1*}Assistant Professor, Department of Kaumarbhritya, Shree Ram Ayurvedic Medical College and Hospital, Meerut, UP.

²Associate Professor, H.O.D. Department of Kaumarbhritya, National Institute of Ayurveda, Jaipur, Rajasthan, India.

ABSTRACT

Balchaturbhadra churna is a poly-herbal formulation used in pediatric practice in Ayurveda especially in the treatment of vomiting, diarrhea, fever and respiratory disorders. The human clinical dose of *Balchaturbhadra churna* is 1000 mg per day. It is prepared by mixing equal proportions of rhizome of *Cyperus rotundus* Linn. (Cyperaceae), fruit of *Piper longum* Linn. (Piperaceae), root of *Aconitum heterophyllum* Wall. ex. Royale. (Ranunculaceae) and gall of *Pistacia integerrima* Stew. Ex. Brandis. (Anacardiaceae). **Aims and objectives:** Critical analysis of *Balchaturbhadra churna* in management of childhood disorder. **Material and Methods:** Various Ayurveda classics and studies published in journals related to use of *Balchaturbhadra churna* in management of childhood disorder are reviewed and analyzed. **Discussion:** Contents of *Balchaturbhadra churna* are mostly *Katu rasa*, *Laghu guna*, *Usna veerya* and also *Deepana*, *Pachana*, *Krimighna*, *Visaghna*, *Hridya*, *Ruchya*, *Vrisya*, *Rasayana*, *Rochana*, *Sthoulyahara*, *Trisnanigrahana*, *Tvakadosahara*, *Jwaraghna* etc. properties. Therefore due to presence of these qualities, it is used in vomiting, diarrhea, fever and respiratory disorders. According to studies published in journals, it is beneficial as immuno-modulator, anti inflammatory, anti spasmodic, anti asthmatic activity, anti bacterial activity, antidiabetic activity, antioxidant activity, anti-fungal activity, hepatoprotective action, analgesic activity. **Conclusion:** Present review reveals *Balchaturbhadra churna* is quite safe for administration among Children and therefore can be used in various ailments in children which can limit the irrational use of antibiotics in them.

KEYWORDS: *Balchaturbhadrachurna*, *Ayurveda*, *Cyperus rotundus*, *Piper longum*, *Aconitum heterophyllum*, *Pistacia integerrima*.

INTRODUCTION

Antibiotic resistance is posing the greatest challenge to medical science. Irrational use of antibiotics has led the Children being more vulnerable, special cares have to be taken in selecting the drugs and formulations. *Balchaturbhadra churna* is a poly-herbal formulation used in pediatric practice in Ayurveda especially in the treatment of vomiting, diarrhea, fever, and respiratory disorders which are the most common childhood morbidities. The human clinical dose of *Balchaturbhadra churna* is 1000 mg per day. It is prepared by mixing equal proportions of the rhizome of *Musta* (*Cyperus rotundus*) Linn. (Cyperaceae), fruits of *Pippali* (*Piper longum*) Linn. (Piperaceae), roots of *Ativisha* (*Aconitum heterophyllum*) Wall. ex. Royale. (Ranunculaceae) and gall of *Karkatashringi* (*Pistacia integerrima* Stew.) Ex. Brandis. (Anacardiaceae).^[1]

It is mentioned in various classical Ayurveda, like *Chakradatta*,^[2] *Bhaishajya ratnavali*^[3] and *Yog ratnakar*,^[4] specifically indicated for respiratory diseases, vomiting, diarrhea and fever in children.

As there is increasing tendency of irrational use of antibiotics in children, this has led to the development of superbugs which do not respond to antibiotics and are posing the greatest challenge to conventional medicines. *Balchaturbhadra churna* is quite effective in various childhood disorders and if used in children can minimize the use of antibiotics. The present paper reviews the effect of *Balchaturbhadra churna* on childhood disorders and provides the clinical and experimental evidences for the same.

Aim Present paper reviews the indications and uses of *Balchaturbhadra churna* described in Ayurveda texts. Studies published in various journals regarding the evidences of its effect are also reviewed. Clinical and experimental efficacy of each ingredient are reviewed and discussed here.

To study the effect of *Balchaturbhadra churna* in childhood diseases with evidences.

Methodology

Table 1: Ingredients and the part used of *Balchaturbhadra churna*

Name of drug	Botanical name	Family	Part used	Proportion
<i>Musta</i>	<i>Cyperus rotundus</i> Linn.	Cyperaceae	Rhizome	1 part
<i>Pippali</i>	<i>Piper longum</i> Linn.	Piperaceae	Fruit	1 part
<i>Ativisha</i>	<i>Aconitum heterophyllum</i> Wall.	Aconitaceae	Root	1 part
<i>Karkatashringi</i>	<i>Pistacia integerrima</i> Stew.	Liliaceae	Gall	1 part

Table 2: Pharmacological properties of the contents of *Balchaturbhadra churna* as per Ayurveda

S.N.	Drug Name	Rasa	Guna	Virya	Vipaka	Doshaghnata	Karma	Therapeutic uses
1	<i>Musta</i> [5] (<i>Cyperus rotundus</i>)	Tikta, Katu.	Laghu	Sheeta	Madhura /Katu	Kaphahara Pittahara	Sothahara ^[6] (anti-inflammatory), <i>Deepana</i> (increases digestive fire), <i>Pachana</i> (digests undigested material), <i>Grahi</i> (absorbing), <i>Jwaraghna</i> (Anti-pyretic), <i>Atisaraghna</i> (Anti-diarrheal) [7-9]	<i>Ajeerna</i> ^[10-11] (Indigestion), <i>Aruchi</i> (tastelessness), <i>Atisara</i> (Diarrhea), ^[12] <i>Jwara</i> (Fever), <i>Kasa</i> (Cough) ^[13-14] <i>Shwasa</i> (Asthma), <i>Vamana</i> (Vomiting), <i>Vatarakta</i> (Gout) ^[15]
2	<i>Ativisha</i> [16] (<i>Aconitum heterophyllum</i>)	Tikta, Katu.	Laghu	Ushna	Katu	Kaphahara Pittahara	<i>Deepana</i> (increases digestive fire), <i>Pachana</i> (digests undigested material), <i>Grahi</i> (absorbing) ^[17]	<i>Jwara</i> (Fever), <i>Chardi</i> (vomiting), <i>Atisara</i> (diarrhea), <i>Shoth</i> (inflammation), <i>Visha</i> (poisoning), <i>Ageerna</i> (indigestion), <i>Kasa</i> (Cough) ^[18-20]
3	<i>Katrkatshringi</i> [21] (<i>Pistacia integerrima</i>)	Tikta, Kashaya	Laghu	Ushna	Katu	Kaphahara Vatahara	<i>Kasahara</i> [22] (anti-tussive), <i>Hikkanigrahana</i> (anti-hiccup) ^[23]	<i>Svasa</i> (asthma), <i>Chardi</i> (vomiting), <i>Hikka</i> (hiccup), <i>Jvara</i> (Fever), <i>Kasa</i> (Cough) ^[24]
4	<i>Pippali</i> [25] (<i>Piper longum</i>)	Katu	Ushna, Snigdha Laghu	Ushna	Madhura	Kaphahara Vatahara	<i>Deepana</i> [26] (increases digestive fire), <i>Hridya</i> [27] (heart disease)	<i>Arsa</i> (hemorrhoid), <i>Hikka</i> (hiccup), <i>Kasa</i> (cough), <i>Prameha</i> (diabetics), <i>Udara Roga</i> (abdominal pain), <i>Jwara</i> (fever) ^[28]

Therapeutic uses of *Balchaturbhadra Churna* [29-31]

Jvaratisara (fever & diarrhea), *Kasa* (cough), *Svasa* (asthma) and *Vamana* (vomiting).

Evidences: Clinical And Experimental

Musta (Cyperus rotundus)

1. Antibacterial activities

The methanol extract of *Cyperus rotundus* studied for antibacterial activity in the microorganism stains of human pathogenic bacteria both gram positive and gram negative bacteria such as *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*. The methanol extract of *Cyperus rotundus* flower showed highly antibacterial activity. [32] The ethanolic extract of the plant was active against all the investigated bacterial strains while the aqueous extract was inactive for *S. typhimurium*. The oil and its fractions hydrocarbon-I and II extracted from *Cyperus rotundus* alcohol fraction-cyperol was found to possess significant antibacterial effect against *Staphylococcus Aureus*. [33] The antibacterial activity of different extracts was determined by agar well-diffusion method. [34] The root extract of *C. rotundus* showed notable antibacterial activity against selected pathogens i.e. *H. influenzae*, *P. aeruginosa*, *S. aureus*, *S. pneumoniae* and *S. pyogenes*. An inhibitory effect of *C. rotundus* was observed against selected bacterial strains including *S. aureus*, *Salmonella enteritidis* and *Enterococcus faecalis* with total oligomers flavonoids and ethyl acetate extracts. [35] Tambekar et al, (2009) also reported that MeOH extract of the rhizomes of *C. rotundus* showed considerable antibacterial potential against *S. aureus*, *K. pneumoniae*, *S. typhi*, *S. paratyphi*, *S. typhimurium*, *P. aeruginosa*, *E. aerogenes*. [36] In a study, maximum inhibition was found against *H. influenzae* (18.4±0.07 mm) followed by *S. pyogenes* (17.3±0.13mm), *P. aeruginosa* (16.2±0.07 mm) and *S. pneumoniae* (15.5±0.15 mm) and minimum against *S. aureus* (15.3±0.05 mm) respectively. [37] The *C. rotundus* extract had antibacterial effects (bactericide and bacteriostatic) on *S. mutans* and *L. acidophilus*. Although this effect was lower than CHX. With regard to adverse effect of CHX, this extract can be a potential antibacterial agent. [38]

2. Anti-inflammatory Activity

To evaluate the anti-inflammatory activity in adult albino wistar rats, *C. rotundus* extract of the tuber part was used. The test group was treated with ether, ethanol, and distilled water extract of three equal portions of the powder. The ethanolic extract showed good anti-inflammatory effect than other solvents system. [39] Phytochemical investigation of the methanolic extract of *Cyperus rotundus* L. (Cyperaceae) rhizomes afforded a new norterpeneoid with an unprecedented carbon skeleton, namely

cyperalin A (1) and sugetriol triacetate (2). The isolated compounds were evaluated for their anti-inflammatory activity. [40]

3. Immunomodulatory activity

Immunomodulatory activity of extracted lectins from rhizome of *Cyperus rotundus* was evaluated on phagocytic activity by carbon clearance test on Albinos Wistar mice at dose of 25mg/kg by intraperitoneal injection (IP). The extracted lectins from rhizome of *Cyperus rotundus* exhibited significantly dose-dependent phagocytic index indicating stimulation of the reticulo-endothelial system. [41] In vitro tests on the ethanol extracts of *C. rotundus* rhizomes shows the extract inhibited leukotrienes production by 66–91% at 30–300 µg/ml. [42]

4. Antioxidant Activity

The evaluation of antioxidant property of ethanolic extract of *Cyperus rotundus* (EECR) was carried out by *in vitro* non-enzymatic glycosylation of hemoglobin method. [43]

5. Anti-diarrheal Activity

The aqueous extract of *C. rotundus* tubers shows anti-giardial activity against infectious diarrhea. [44] The decoction of *C. rotundus* tubers also showed anti-diarrheal activity and effect on adherence of enteropathogenic *E. coli*, *entero invasive E. coli* and *Shigella flexneri* to Hep-2 cells. [45]

6. Antiulcer Activity

The antiulcer activity of *C. rotundus* tuber powder extract was investigated in two different animal models. The first one was histamine-induced ulcer in guinea pigs, and another one was aspirin-induced gastric mucosal damage in rats. In the both cases, the plant extract showed maximum reduction of ulcer which was comparable to ranitidine. [46]

7. Antidiabetic Activity

The antidiabetic activities of hydro alcoholic extract of *C. rotundus* rhizomes were studied on Sprague-Dawley rats. Alloxan monohydrate was administered intraperitoneally to induce diabetes which showed significant rise in the blood glucose level. On the 15th day, after administration of the plant extract, the blood glucose level reduced as compared to the metformin. This observation suggests that the aqueous ethanolic extract of *C. rotundus* rhizomes have significant hypoglycemic activity. [47]

8. Anti-allergic Activity

Sesquiterpenes isolated from the ethanolic extract of the rhizomes of *C. rotundus* (CRE) were observed to possess anti-allergic activity. It was found that sesquiterpenes inhibited the 5-LOX catalyzed production of leukotrienes (LTs). Also they inhibited β-hexosaminidase release, as well as its

degranulation. The delayed type hypersensitivity reaction was also delayed by valencene and nootkatone present in the CRE. [48]

9. Ovicidal and Larvicidal Effect

The ovicidal and larvicidal effects of essential oil of *C. rotundus* extracted by hydrodistillation on eggs, and fourth instar larvae of *Aedes albopictus* were identified. It was observed that the essential oil possesses ovicidal and larvicidal property when exposed to serial concentrations ranging from 5 to 150 ppm. [49]

Pippali (*Piper longum*)

1. Antibacterial activity

The essential oil of *Piper longum* showed antibacterial activity against *B. cereus*, *B. subtilis*, *M. tuberculosis*, *Staph. albus*, *Staph. Aureus*, and *B. shigella dysenteriae*, *Esch.Coli*, *Sh. boydi*, *Sal. typhi* and *Vib. cholerae*. The oil was more active than the oils of *Alpinia galanga*, *Nigella sativa*, *Vateria indica* and *Saccopetalum tomentosum*. [50] Dry roots of the plant *Piper longum* were extracted with n-hexane. The constituents were isolated and purified by column chromatography. The structures of the isolated constituents were confirmed by spectral analysis. The isolated constituents and n-hexane extract were found to show varying degree of antibacterial activity against all the tested bacteria. However, the aqueous extract did not show antibacterial activity against the tested bacteria. The isolated constituents were found to show better activity profile than the n-hexane extract, which indicates that the isolated constituents might be responsible for the antibacterial activity. [51]

2. Anti allergic activity

In an experimental study, albino rats were sensitized with horse serum. The rats were treated with ethanolic extract of Pippali (*Piper longum*) for 14 days. The result showed that the extract at 100 and 200 mg/kg bodyweight inhibited degranulation of mast cells to an extent of 62.44 and 67.24 % respectively. [52] The milk extracts of the fruits of Pippali (*Piper longum*), reduced passive cutaneous anaphylaxis in rats and protected guinea pigs against antigen-induced bronchospasm. [53] The petroleum ether extract of *P. longum* produced respiratory stimulation in smaller doses in various species. [54] Morphine and pentobarbitone induced respiratory depression was antagonized by the extract. [55]

3. Anti asthmatic activity

The effect of petroleum ether, alcoholic extracts and decoction of the fruits of Pippali (*Piper longum*) was studied for antihistaminic activity on Guinea pigs. At the dose of 100 µ g/kg bodyweight the extracts significantly inhibited the release of

histamine from mast cells. The extracts at 50, 100 and 200 mg/kg bodyweight protected the animals from histamine induced bronchospasm. This effect was dose dependent and therefore Pippali (*Piper longum*) is supposed to prevent the development of bronchial asthma. [56]

4. Immunomodulatory activity

Haemagglutination titre, macrophages migration index (MMI) and phagocytic index (PI) in mice demonstrated immunostimulatory action of *Piper longum* fruits to be both specific and non specific. The effects was more prominent in lower doses (225 mg/kg) and was marginally reduced when the dose was increased," In another study, it was found to offer protection against externally induced stress," A famous Ayurvedic compound containing long pepper, pippali rasayan was tested in mice infected with *Giardia lamblia* which was found to produce significant activation of macrophages as shown by an increased macrophage migration index (MMI) and phagocytic activity. [57]

5. Antispasmodic action

The crude extract of *Piper longum* as well as pipartine suppressed the ciliary movements of the esophagus of frog. These findings suggest that therapeutic efficacy in relieving cough could be due to the suppression of cough reflex. [58] Also the milk extract of *P. longum* effectively reduced passive cutaneous anaphylaxis in rats and guinea pigs; protected guinea pigs against antigen induced bronchospasm. [59-60]

6. Larvicidal Effect

Some of the piper species, *P. longum*, *P. guanacastensis* and their bioactive constituents are reported to have remarkable larvicidal activity against various mosquito species such as *Cx. pipiens pallens*, *Ae. aegypti*, *Ae. togoi* and *Ae. atropalpus*. [61-62]

7. Anti-fungal activity

The essential oil of *Piper longum* demonstrated anti-fungal activity against *Aspergillus flavus*, *Trichoderma viridi*, *Curvularia lunata*, *Penicillium javanicum* and *P. striatu*. [63]

8. Anti-inflammatory activity

A marked anti-inflammatory activity of *Piper longum* fruit decoction against carrageenin induced rat paw oedema was reported. [64] By Ammonium sulphate precipitation method a protein was isolated from Pippali (*Piper longum*). This protein showed anti-inflammatory, antioxidant and free radical scavenging activity *in vitro*. At a dose of 1000µg/ml the Pippali (*Piper longum*) showed maximum anti-inflammatory activity which was similar to that of Diclofenac sodium. [65] Four different market samples

of each variety of Pippali were procured from different regions of India. The samples collected from South India which have given more extractive values were selected for screening of anti-inflammatory activity. Randomly selected animals were divided into four groups of six animals each. The test drugs were administered orally at a dose of 200 mg/kg and the activity was compared with standard anti-inflammatory drugs in both models. [66]

10. Antioxidant activity

Using aqueous extract of Pippali (*Piper longum*) fruit, silver nanoparticles were synthesized. These nanoparticles showed powerful antioxidant activities. Furthermore this activity was found to be similar to the standard antioxidants like vitamin E and butylated hydroxyanisole (BHA). [67]

11. Hepatoprotective activity

In a study, ethanol, petroleum ether, solvent ether, ethyl acetate, butanol and butanone extracts of the fruits of pippali (*Piper longum*) were evaluated for their hepatoprotective activities in adult Wistar rats. The ethanolic and butanol fractions showed a significant hepatoprotective activity. The results were compared to control and Liv-52-treated rats. [68]

Ativisha (*Aconitum heterophyllum*)

1. Antibacterial activity

Antibacterial activities are found against gram negative (diarrhea causing) bacteria *Escherichia coli*, *Shigella fl exineri*, *Pseudomonas aeruginosa* and *Salmonella typhi*. [69] *A. heterophyllum* plant has been reported to hold antifungal, cytotoxic, antiviral and immune-stimulant properties along with anti bacterial properties. [70-72] The alkaloid extract *Aconitum heterophyllum* showed significant level of antibacterial activity against *S. aureus*, *B. bronchiseptica*, *B. subtilis*, *P. putida* and *X. campestris* at higher concentration of 100 µg/ disc. The alkaloid extracts showed bactericidal effect against *S. aureus*, *B. bronchiseptica* and *B. subtilis*, whereas bacteriostatic effect was observed against *P. putida* and *X. campestris*. [73] Two new aconitine-type norditerpenoid alkaloids 6-dehydroacetyl-sepaconitine (1) and 13-hydroxylappaconitine (2), along with three known norditerpenoid alkaloids lycocotonine, delphatine and lappaconitine were isolated from the roots of the *Aconitum heterophyllum* Wall, both of which exhibited significant antibacterial activity. [74]

2. Anti-inflammatory activity

The anti-inflammatory and analgesic activities of higenamine (a plant-based alkaloid) were evaluated by measuring paw edema. It was found to possess significant anti-inflammatory activity in the dose range of 10-50 mg/kg and good analgesic activity at

the dose of 200 mg/kg. [75] Also the ethanolic root extract of *Aconitum heterophyllum* demonstrated the anti-inflammatory properties comparable to diclofenac sodium at dose of 900 mg/kg. [76]

3. Immunomodulatory activity

The ethanolic extract of *Aconitum heterophyllum* tuber enhanced the phagocytic function and inhibited the humoral component of the immune system, therefore showing immunomodulatory activity. [77]

4. Antioxidant activity

In vitro antioxidant activity of root extract of *Aconitum heterophyllum* was found to be equal to Vitamin C and in an in vivo study root extract treated animals showed significant attenuation of biochemical parameters and histo-pathological changes of the kidney compared to glycerol treated group and it was found to be more significant with the extract at 500 mg/kg than 250mg/kg. [78]

5. Immunomodulatory activity

For treatment of chronic infections and immunological disorders, the immunobiological activity was investigated of certain medicinal plants commonly used in the Ayurvedic and Unani systems of medicine. The effect of an ethanolic extract of each drug was considered on delayed type hypersensitivity, humoral responses to sheep red blood cells, skin allograft rejection, and phagocytic activity of the reticulo-endothelial system in mice. *Aconitum heterophyllum* appeared to stimulate phagocytic function while inhibiting the humoral component of the immune system. [79]

Karkatshrungi (*Pistacia intergerrima* stew. Ex. Brandis)

1. Antibacterial activity

The *Pistacia intergerrima*, *Cedrus deodara* and *Gymnema sylvestre* are active against seven different microorganisms like *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas*, *Bacillus subtilis* and *Staphylococcus aureus* by using disc diffusion method. properties of all the phytochemicals were present in *Pistacia intergerrima*, so demonstrated higher antibacterial activity. Comparison of standard antibiotic (teracyclin) was done with efficacy of plant extract which showed variable inhibitory activity against each bacterium. [80] *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* (*S. aureus*), methicillin resistant *S. aureus* and vancomycin resistant *S. aureus* along with standard bacterial strains were used. Significant inhibitions by gall extracts which were acquired by extraction procedures with five solvents had been recorded for these multiple drug resistance (MDR) bacteria. The galls extract with water and Chloroform

had shown greater antibacterial activity against bacteria.^[81] The chloroform fractions of *Debregeasia salicifolia* & *Toona ciliate*, methanol fraction of *Pistacia integerrima*, and aqueous fraction of *Aesculus indica* are suitable for the development of novel antibacterial compounds.^[82]

2. Antiasthmatic activity

A dose dependent effect on disruption rate of actively sensitized mesenteric mast cells of albino rats was demonstrated upon treatment with aqueous extract of galls when challenged with antigen (horse serum along with triple antigen vaccine). The significant protection against histamine aerosol-induced bronchospasm in guinea pigs was shown with treatment of aqueous extract of galls for ten days and also showed the spasmolytic activity against histamine induced contractions in isolated guinea pig tracheal chain preparation. It demonstrated the antiasthmatic activity of aqueous extract of *P. integerrima* galls.^[83] The anti-asthmatic activity of *Pistacia integerrima* may be attributed to reduction in TNF- α , IL-4, and IL-5 expression levels, and increase in AQP1 and AQP5 expression levels.^[84]

3. Antioxidant activity

Essential oil of *Pistacia integerrima* J.L. Stewart ex Brandis galls (EOPI) was tested using in vitro studies such as antioxidant activity, mast cell degranulation, angiogenesis, isolated guinea pig ileum preparation and soyabean lipoxidase enzyme activity. In vivo studies showed airway hyper-responsiveness in ovalbumin in sensitized guinea pigs using spirometry and lipopolysaccharide-induced bronchial inflammation in rats.^[85] The crude extract and sub fractions of *Pistacia integerrima* galls were evaluated for their antioxidant potential using ABTS and DPPH assays.^[86] Acetone extract exhibited highest total phenolics contents (113.7 mg GAE/100g, FW) and antioxidant potential for ferric ion reduction (107.3 μ M GAE/100g, FW), phosphomolybdenum complex assay (99.32 μ M AAE/100g, FW) and DPPH radical scavenging (91.89%). Fruit of *P. integerrima* was shown to have excellent properties of nutrients, minerals and antioxidants. Crude extracts *P. integerrima* showed noteworthy potential against free radicals and could be of immense significance in the prevention of different diseases related to free radicals.^[87]

4. Radical scavenging activity (DPPH)

Ethyl acetate and Butanol fractions of *P. integerrima* are reported to be enriched with monoglycosides and polyglycosides which showed higher antiradical activity as compared to aqueous and ethanol extracts. The active phytoconstituents isolated from *P. integerrima* extract showed significant antioxidant activity. The flavonoids and

phenolic compounds present in the extracts of *P. integerrima* leaves have good radical scavenging and xanthine oxidase inhibitory activity.^[88]

5. Anti-inflammatory effect

Anti-inflammation and analgesic activities of six tetracyclic, triterpenoids, pistaci gerrimones A, B, C, D, E, and F isolated from gall of *P. integerrima* was demonstrated. Pistaci gerrimones C and D exhibited highly significant activities showing an inhibition of paw oedema between 30-70% at a dose, 5 mg/kg.^[89] The extracts of *Pistacia integerrima* 50-200 mg/kg (p.o.) had modest activity against hind paw acute and chronic inflammation induced by formalin ($P < 0.01$).^[90] The flavonoids (1-4) isolated from the chloroform fraction of *Pistacia integerrima* galls had anti-hyperalgesic and anti-inflammatory effects. The pretreatment of flavonoids (1-4) elicited marked anti-inflammatory effects in carrageenan induced paw edema test in mice during various assessment times (1-5 h).^[91]

6. Analgesic activity

Pistacia integerrima barks contain good analgesic properties. The analgesic properties of traditional medicine are recognized through biologically active compounds which are the secondary metabolites of plants such as glycosides, tannins, flavonoids, alkaloids, saponins which are responsible for therapeutic properties of the plants like analgesic, anti-inflammatory and antipyretic. Flavonoids are known to target prostaglandins involved in acute inflammation and pain perception and flavonoids have therefore been accounted for analgesic, anti-inflammatory and antipyretic activities.^[92] *Pistacia integerrima* extracts have anti-nociceptive and analgesic effects and did not reveal to have acute toxicity on oral administration.^[93]

Effect of Balchaturbhadra Churna

The *Balchaturbhadra Churna* did not modify humoral antibody formation, relative weight of spleen and the thymus of albino rats to significant extent. Immunological odema represents cell mediated immune response hence it can be inferred that the *Balchaturbhadra Churna* produces significant suppression of cell mediated immunity which is direct correlation of delayed type hypersensitivity (DTH) response and do not influence humoral immune response. The observed effect may be the main mechanism for the efficacy of the drug in respiratory disorders (Parmar, et.al., 2011).

Dose:

The dose for the experimental study was calculated by extrapolating the clinical human dose of *Balchaturbhadra churna* (1000 mg per day) to an animal dose based on body surface area ratio by

using conversion factor of 0.018.^[94] The histopathological studies of 16 organs showed that *Balchaturbhadra churna* at 450 mg/kg, increased the cellularity in the thymus and spleen. Other organs exhibited normal cytoarchitecture suggesting that the preparation is devoid of serious organ degenerative potential at this dose level. At the higher dose of 900 mg/kg changes were observed in the spleen, thymus, and testis. The white pulp (lymphatic tissue) of the spleen forms a sheath around the arteries. The stroma is a network of reticular fibers and phagocytic reticular cells or fixed macrophages. As in all lymphatic tissue, the meshes of the framework are filled with free lymphocytes of various sizes, distributed to form diffuse and nodular lymphatic tissue which vary continuously and reflect the reaction of lymphatic tissue to various generalized stimuli.^[95]

Toxicological Assessment of the drug^[96]

Acute toxicity test: *Balchaturbhadra churna* did not generate any signs or symptoms of toxicity or mortality up to a dose of 2000 mg/kg which is more than 20 times more than therapeutic equivalent dose in rats, obviously indicating that the formulation is suspect to induce any drastic toxic effect in spite of containing *Aconitum heterophyllum*.

Long-term toxicity test: The effect of *Balchaturbhadra churna* on various parameters such as percentage change in body weight, on the hematological parameters, on serum biochemical parameters, on biochemical parameters, and histopathological studies showed no harmful effect and did not generate any adverse effect on the above parameters except heavy dosage which was very much larger than actual therapeutic dose.

CONCLUSION

Present review reveals that *Balchaturbhadra churna* is quite safe for administration among children and can provide better result in diseases of vomiting, diarrhea, fever and respiratory disorders both as prophylactic and curative medication due to its *Katu rasa*, *Laghu guna* and *Usna virya* according to Ayurveda. A large number of research studies reveal that constituents of *Balchaturbhadra churna* is beneficial as immuno-modulator, anti-inflammatory, anti spasmodic, anti asthmatic activity, anti bacterial activity, antidiabetic activity, antioxidant activity, anti-fungal activity, hepatoprotective action, analgesic activity. This undoubtedly solves the safety concerns related to the presence of *Aconitum* species drug in the formulation. *Balchaturbhadrachurna* is quite safe for administration among Children and therefore can be used in various ailments in children which can limit the irrational use of antibiotics in them.

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***Address for correspondence**

Dr Nitu Sinha

Assistant Professor,
Department of Kaumarbhritya,
Shree Ram Ayurvedic Medical
College and Hospital, Meerut, UP
Email: ntsinha920@gmail.com

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