Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Ethnopharmacology 96 (2005) 445–449
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Efficacy of *Tinospora cordifolia* in allergic rhinitis

V.A. Badar[a], V.R. Thawani[b,*], P.T. Wakode[c], M.P. Shrivastava[a], K.J. Gharpure[b], L.L. Hingorani[d], R.M. Khiyani[e]

[a] *Department of Pharmacology, Indira Gandhi Medical College, Nagpur 440018, India*
[b] *Department of Pharmacology, Government Medical College, Nagpur, India*
[c] *Department of ENT, Indira Gandhi Medical College, Nagpur, India*
[d] *Pharmanza, India*
[e] *Government Ayurvedic College, Nagpur, India*

Received 23 February 2004; accepted 17 September 2004
Available online 23 November 2004

Abstract

The efficacy of *Tinospora cordifolia* (TC) extract in patients of allergic rhinitis was assessed in a randomized double blind placebo controlled trial. Seventy-five patients were randomly given either TC or placebo for 8 weeks. They were clinically examined and Hb %, TLC, DLC and nasal smear was done. At the end of trial baseline investigations were repeated, drug decoded and results analyzed. With TC treatment 100% relief was reported from sneezing in 83% patients, in 69% from nasal discharge, in 61% from nasal obstruction and in 71% from nasal pruritus. In placebo group, there was no relief in 79% from sneezing, in 84.8% from nasal discharge, in 83% from nasal obstruction, and in 88% from nasal pruritus. The difference between TC and placebo groups was highly significant. TLC increased in 69% patients in drug treated group and in only 11% with placebo. After TC, eosinophil and neutrophil count decreased and goblet cells were absent in nasal smear. After placebo, decrease in eosinophil and neutrophil count was marginal and goblet cells were present. TC significantly decreased all symptoms of allergic rhinitis. Nasal smear cytology and leukocyte count correlated with clinical findings. TC was well tolerated.

Keywords: Herbal extract; Immunostimulation

1. Introduction

Allergic rhinitis is the commonest atopic disease with prevalence of 5–22% (Smith, 1988). It is the sixth most prevalent condition in the US, outranking cardiac disease (Collins, 1988). It is characterized by sneezing, rhinorrhea, nasal congestion and pruritus of nose and eyes. The disease and its complications like sinusitis, eustachian tube dysfunction, sleep disturbance and the consequences of chronic mouth breathing are responsible for morbidity and absenteeism. Allergic rhinitis begins at any age but peak incidence is during the childhood–adolescence. The incidence is higher in those whose parents have positive history of the disease.

Allergic rhinitis implies hypersensitive response following exposure to allergens including pollens of grass, weeds, trees, animal danders, house dust and food. Rhinitis symptoms impair patients' quality of life (Bousquet et al., 1994). Antihistamines, decongestants, cromolyn sodium, glucocorticoids are routinely used in the control of allergic rhinitis (Naclerio, 1991). H_1 antagonists which are commonly used, produce drowsiness and CNS depression. The newer generation of H_1 antagonists is devoid of drowsiness but have other side effects. Hence the search for an effective, safer, better tolerated alternative, which is natural. It has been suggested that when routinely used pharmacological interventions fail to relieve the symptoms, allergen immunotherapy may be effective (Kalra et al., 2002).

* Corresponding author. Present address: 14-A, Jeevan Jyoti, Clarke Town, Nagpur 440004, India. Tel.: +91 712 2522977/2557744; fax: +91 712 2559060.
E-mail address: thawani_ngp@sancharnet.in (V.R. Thawani).

0378-8741/$ – see front matter © 2004 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2004.09.034

Tinospora cordifolia (Willd) Miers is a deciduous climbing shrub indigenous to tropical Indian subcontinent, belonging to the family Menispermaceae. In Indian vernacular the plant is known as Giloya, meaning heavenly elixir, which saved celestial beings from old age and kept them eternally young. It is widely used in veterinary medicine and in Ayurveda for its general tonic, antispasmodic, anti-inflammatory, antiarthritic, antiallergic and antidiabetic effects (Sharma et al., 2001). In Ayurveda *Tinospora cordifolia* is used as "rasayana" (Thatte and Dahanukar, 1997) which in Sanskrit implies—circulation of "rasa"—the nutrient. The ancient Indian physician, Charaka described rasayana as antiaging, increasing the life span, promoting intelligence, improving memory and freedom from diseases, indicating immunostimulant effect (Sharma, 1981).

This study was planned to scientifically validate the efficacy of TC in allergic rhinitis patients.

2. Material and method

This was a randomized, double blind, placebo controlled trial. The trial procedure was in accordance with the guidelines of the Declaration of Helsinki and Tokyo. Ethical permission was obtained from Institutional Ethics Committee of Indira Gandhi Medical College, Nagpur. Patients diagnosed to be suffering from allergic rhinitis in the ENT out patient department of the hospital, were approached with request to participate in the trial. Those who showed interest were supplied with detailed information sheet about the trial, in language understood by them. From those who volunteered to participate, informed witnessed written consent was taken. The inclusion and exclusion criteria were:

2.1. Inclusion criteria

- Subjects diagnosed to be suffering from allergic rhinitis.
- Volunteering to participate and give signed informed consent.
- Of either gender.
- In age range of 18–60 years.

2.2. Exclusion criteria

- Pregnant and lactating women.
- Clinical evidence of bacterial sinusitis.
- Associated chronic diseases like hypertension, ischemic heart disease, diabetes, psychiatric and CNS disorders.
- Consuming concurrent medication for chronic diseases.
- Alcoholics and drug addicts.
- Having cyanosis, clubbing or lymphadenopathy.
- Within 6 weeks of having received antihistaminic or steroid therapy.

M/s Pharmanza (India) supplied the active drug and matching placebo. Each tablet of TC (Tinofend)® contained 300 mg of standardized extract obtained from water extract of stem of TC. It contained more than 5% bitter principles and was tested for presence of cordioside and tinosporoside by HPLC.

After clinical examination by ENT surgeon, Hb %, TLC, DLC and nasal smear (Wakode et al., 1989) were done to get the baseline data. Pulse, respiratory rate, blood pressure and temperature were recorded. X-ray of paranasal sinuses was done to rule out sinusitis in suspected cases. Patients suffering from acute sinusitis were treated with antibiotics for 1 week followed by wash out of 1 week and later entered in the trial. All data was logged in case record form by chief investigator.

Seventy-five participants were randomly allocated totaling 37 to group A and 38 to group B, to either receive coded TC 300 mg one tablet thrice daily or matching placebo in the same formulation, packing, size, weight, color and dose for 8 weeks. The drug was issued to patients for duration of fortnight at a time. The patients were asked to bring the unused drugs and container during the follow up. Eighty percent consumption was considered to be compliant. The returned drugs were discarded. After completion of the 8 weeks study period, all baseline investigations were repeated. The participants were followed up for 1 month after stoppage of the drug. At the end of the study period the drug was decoded and the results calculated by Fisher's exact test and Chi-square test.

As rescue medication, initially H_1 antagonist and later antibiotics were allowed. The patients were at liberty to withdraw from the trial anytime. During the trial one patient developed sinusitis requiring antral puncture. She was dropped from the trial and after decoding, was found to be on TC. Three patients opted out of the trial because of lack of relief from symptoms. After decoding they were found to be from the placebo group.

3. Observations

It was seen that allergic rhinitis was more common in the age group 20–30 years (66.20%). There were 11 patients in the age group of 30–40 (15.50%), 8 in 40–50 (11.26%) and 5 in 50–60 age group (7.04%). Women were more affected than men (48:27). On clinical examination it was found that 44 had inferior turbinate hypertrophy and 10 had middle turbinate hypertrophy. Middle septum was central in 46, to the right in 15 and to the left in 9 patients. Nasal mucosa was pale blue in 66 patients. Nasal discharge was seen in 68 (90.66%), sneezing in 64 (85.33%), nasal obstruction in 62 (82.66%) and pruritus in 53 (70.66%). In active TC treated group clinical exam revealed change in color of mucosa from blue to pink in 69% patients.

4. Results

Allergic rhinitis was found to be more common in the age range of 20–30 and women. On analyses of the effect

Table 1
Percentage improvement in symptoms of allergic rhinitis

Percentage improvement in symptoms	*Tinospora cordifolia* extract ($n = 36$)[a]				Placebo ($n = 35$)			
	100	75	50	0	100	75	50	0
Nasal discharge (TC 35, placebo 33)[b]	68.57 (24)	22.86 (8)	5.71 (2)	2.86 (1)	3.03 (1)	0.00	12.12 (4)	84.85 (28)
Sneezing (TC 35, placebo 29)	82.86 (29)	14.28 (5)	2.86 (1)	0.00	3.45 (1)	6.90 (2)	10.34 (3)	79.31 (23)
Nasal obstruction (TC 33, placebo 29)	60.61 (20)	0.00	33.33 (11)	6.06 (2)	0.00	3.45 (1)	13.79 (4)	82.76 (24)
Nasal pruritus (TC 28, placebo 25)	71.43 (20)	0.00	25.00 (7)	3.57 (1)	0.00	4.00 (1)	8.00 (2)	88.00 (22)

TC: *Tinospora cordifolia* extract; $p < 0.00001$.
[a] Figures in parenthesis show the number of patients.
[b] Presence of symptom before drug therapy in respective groups, after decoding.

Table 2
Percentage change in total leukocyte count (TLC) due to intervention[a]

Change in TLC	*Tinospora* ($n = 36$)	Placebo ($n = 35$)
Increase	69.44 (25)	11.43 (4)
Decrease	25.00 (9)	14.28 (5)
No change	5.56 (2)	74.29 (26)

$p < 0.001$.
[a] Figures in parenthesis show the number of patients.

of TC and placebo after 8 weeks of administration on the symptoms of allergic rhinitis (Table 1), it was seen that there was total relief from sneezing in nearly 83% patients who received TC while in placebo group 79% had no relief at all. In case of nasal discharge, TC showed 100% improvement in nearly 69% while in placebo group only one patient (3.03%) had such relief. Nasal obstruction was totally cleared in nearly 61% patients who had received TC while nearly 83% patients on placebo had no relief from it. In nasal pruritus, 71% patients of TC group had 100% improvement whereas in placebo group 88% had no relief from this symptom. On comparison, the difference between TC and placebo treated groups in all the symptoms of allergic rhinitis viz. sneezing, nasal discharge, nasal obstruction and nasal pruritus, was found to be highly significant ($p < 0.00001$).

In TC treated group, there was increase in total leukocyte count in 69% patients (Table 2), while in placebo group such increase was seen in only11%. This difference between TC and placebo group was significant ($p < 0.001$).

In nasal smear, after TC treatment, eosinophil and neutrophil count decreased strikingly, while goblet cells were absent (Table 3). In placebo treated patients the decrease in eosinophil and neutrophil count was marginal and goblet cells continued to be there even after 8 weeks ($p < 0.05$).

With TC there was change in the color of nasal mucosa from bluish to pink in 69% patients.

5. Discussion

Allergy is an altered state of the host after contact with specific antigen. Individuals with allergic rhinitis have IgE antibodies that bind to high affinity receptors on mast cells and basophils, and other cells like eosinophils, monocytes and platelets (Tada and Ishizaka, 1970; Melewicz and Spiegelberg, 1980; Grangette et al., 1989). On nasal re-exposure to antigen in allergic rhinitis, the mast cells degranulate, releasing various mediators of inflammation (Gomez et al., 1986), causing itching, sneezing, nasal discharge and congestion in more than 90% of the patients. Nasal challenge induces immediate and delayed response in the form of recurrence of symptoms characterized by influx of eosinophils, neutrophils, basophils and mononuclear cells (Bascom et al., 1988a, 1988b). The eosinophils are reduced by treatment with topical steroids and immunotherapy (Mygind et al., 1978; Furin et al., 1991).

Table 3
Nasal smear cytology (%) in allergic rhinitis patients[a]

	Tinospora cordifolia ($n = 36$)			Placebo ($n = 35$)		
	M	F	O	M	F	O
Eosinophil						
Pre	13.88 (5)	5.55 (2)	19.44 (7)	17.14 (6)	5.71 (2)	11.42 (4)
Post	0.00	8.33 (3)	8.33 (3)	11.42 (4)	5.71 (2)	11.42 (4)
Neutrophil						
Pre	13.88 (5)	19.44 (7)	5.55 (2)	17.14 (6)	11.42 (4)	14.28 (5)
Post	0.00	8.33 (3)	5.55 (2)	11.42 (4)	8.57 (3)	5.71 (2)
Goblet cells						
Pre	0.00	8.33 (3)	5.55 (2)	0.00	5.71 (2)	0.00
Post	0.00	0.00	0.00	0.00	5.71 (2)	0.00

Pre: baseline values before drug administration; post: after 8 weeks of run-in of interventional drug. $p < 0.05$.
[a] Figures in parenthesis indicate number of patients; M: many, F: few, O: occasional.

TC is known to have powerful immunostimulant effect (Dahanukar and Thatte, 1997). Being a rasayana, it increases leukocyte count and ablates neutropenia following single or multiple doses of cyclophosphamide (Thatte et al., 1987; Thatte and Dahanukar, 1988). Pretreatment with TC affords protection against induced infections in mice (Thatte et al., 1992) and rats (Dahanukar et al., 1988). The phagocytic and intercellular bactericidal capacity of polymorphs of TC treated mice is significantly greater (Thatte et al., 1992). The aqueous extract of TC stimulates peritoneal macrophage in a dose dependent manner (Rege and Dahanukar, 1993), suggesting that global activation of macrophage system is essential for the non-specific effects of TC. The primary target of TC is believed to be the macrophages, which play key role in the generation of immune response.

TC decreased the histamine-induced bronchospasm in guinea pigs, decreased capillary permeability in mice and reduced number of disrupted mast cells in rats (Nayampalli et al., 1982; Nayampali et al., 1986). In patients with obstructive jaundice, addition of TC to routine surgical procedure increased the survival rate and also increased polymorphonuclear leukocyte functions (Bapat et al., 1995).

A herbo-mineral preparation containing TC, *Rubia cordifolia* and six other ingredients showed promising antiallergic activity in case of rhinitis, which was devoid of side effects, even after long-term use (Grewal et al., 1985). We used TC as a single ingredient, which increased leukocytes significantly.

In our study, there was a significant improvement in the allergic rhinitis symptoms of sneezing, nasal obstruction, nasal discharge and pruritus. These findings correlated well with clinical finding of change in color of nasal mucosa from bluish to pink in patients on TC. Pink coloration along with symptomatic improvement is considered to be sign of good response (Grewal et al., 1985).

The patients who were on TC were satisfied with the treatment, with only one dropout from the study group due to development of sinusitis in early weeks of the trial. No patient from the TC group went for the rescue medicine. As compared to this the patients from placebo group constantly complained of no relief of symptoms and needed continuous counseling to continue with the study. In the placebo group, there were three dropouts and three patients asked for rescue medication, when the symptoms were bothersome.

In our study out of 36 patients who took TC for 8 weeks, two complained of nasal pain and one had headache, which responded to analgesics. None required discontinuation of TC treatment due to these adverse effects. TC otherwise was well tolerated.

The significant increase in the leukocyte count in our study is suggestive of immunostimulant action of TC. Decrease in goblet cells and eosinophils are indicative of antiallergic effect of TC. Decrease in neutrophils is suggestive of anti-inflammatory effect.

6. Conclusion

Immunostimulation is a known pharmaco-therapeutic intervention in disease management. *Tinospora cordifolia* extract, a plant derived immunostimulant, significantly decreased ($p < 0.00001$) symptoms of allergic rhinitis like sneezing, nasal discharge, nasal obstruction and nasal pruritus. The nasal smear cytology, leukocyte count and clinical findings validated efficacy of TC. Because of its high efficacy, excellent tolerability and absence of serious adverse reactions *Tinospora cordifolia* could be an important constituent of the treatment of allergic rhinitis.

References

Bapat, R.D., Rege, N.N., Koti, R., Desai, N.K., Dahanukar, S.A., 1995. Can we do away with percutaneous trans hepatic biliary drainage? HPB Surgery 9, 5–11.

Bascom, R., Wachs, M., Naclerio, R.M., Pipkorn, U., Galli, S.J., Lichtenstein, L.M., 1988a. Basophil influx occurs after nasal antigen challenge: effects of topical corticosteroid pretreatment. The Journal of Allergy and Clinical Immunology 81, 580–589.

Bascom, R., Pipkorn, U., Lichtenstein, L.M., Naclerio, R.M., 1988b. The influx of inflammatory cells into nasal washings during the late response to antigen challenge: effect of systemic steroid pretreatment. American Review of Respiratory Diseases 138, 406–412.

Bousquet, J., Bullinger, M., Fayol, C., Marquis, P., Valentin, B., Burtin, B., 1994. Assessment of quality of life in patients with perennial allergic rhinitis. The Journal of Allergy and Clinical Immunology 94, 182–188.

Collins, J.G., 1988. National Centre for Health Statistics. Prevalence of selected chronic conditions, United States 1983–1985. Advance data from vital and health statistics no. 155, Hyattsville, MD, Public Health Service, 88-1250.

Dahanukar, S.A., Thatte, U.M., Pai, N.R., More, P.B., Karandikar, S.M., 1988. Immunotherapeutic modification by *Tinospora cordifolia* of abdominal sepsis induced by caecal ligation in rats. Indian Journal of Gastroenterology 7, 21–23.

Dahanukar, S.A., Thatte, U.M., 1997. Current status of Ayurveda in phytomedicine. Phytomedicine 4, 297–306.

Furin, M.J., Norman, P.S., Creticos, P.S., 1991. Immunotherapy decreases antigen induced eosinophil cell migration into the nasal cavity. The Journal of Allergy and Clinical Immunology 88, 27–32.

Gomez, E., Corrado, O.H., Baldwin, D.L., Swanston, A.R., Davies, R.J., 1986. Direct vivo evidence for mast cell degranulation during allergen induced reactions in man. The Journal of Allergy and Clinical Immunology 78, 637–645.

Grangette, C., Gruart, V., Ouaissi, M.A., 1989. Ig E receptor on human eosinophils (Fc_1 RII): comparison with B cell CD 23 and association with an adhesion molecule. Journal of Immunology 143, 3580–3588.

Grewal, D.S., Sharma, B.K., Shah, D.D., Sheode, J.H., 1985. Septilin and geriforte in allergic and vasomotor rhinitis. Auris, Nasus, Larynx (Tokyo) 12, 95–101.

Kalra, S., Wadhwa, P., Kalra, N., 2002. Rhinitis: recent advances. Hospital Today 7, 461–463.

Melewicz, F.M., Spiegelberg, H.L., 1980. Fc receptors for Ig E on a subpopulation of human peripheral blood monocytes. Journal of Immunology 125, 1026–1031.

Mygind, N., Sorensen, H., Pedersen, C.B., 1978. The nasal mucosa during long term treatment with beclomethasone cipropionate aerosol: a light and scanning electron microscopic study of nasal polyps. Acta Otolaryngology (Stockholm) 85, 437–443.

Naclerio, R.M., 1991. Drug therapy in allergic rhinitis. New England Journal of Medicine 12, 860–869.

Nayampalli, S.S., Ainapure, S.S., Nadkarni, P.M., 1982. Study of antiallergic and bronchodilator effects of *Tinospora cordifolia*. Indian Journal of Pharmacology 14, 64–66.

Nayampali, S.S., Desai, N.K., Ainapure, S.S., 1986. Antiallergic properties of *Tinospora cordifolia* in animal models. Indian Journal of Pharmacology 18, 250–252.

Rege, N.N., Dahanukar, S.A., 1993. Quantitation of microbicidal activity of mononuclear phagocytes: an in-vitro technique. Journal of Postgraduate Medicine 39, 22–25.

Sharma, P.V., 1981. Charak Samhita. Chikitsasthana, vol. 2. Chaukhamba Orientalia, Varanasi, India, pp. 62–74.

Sharma, P.C., Yelne, M.B., Dannia, T.J., 2001. Database on medicinal plants used in Ayurveda, vol. 3. Central Council for Research in Ayurveda and Siddha, Government of India, New Delhi, pp. 256–281.

Smith, J.M., 1988. Epidemiology and natural history of asthma, allergic rhinitis and atopic dermatitis (eczema). In: Middleton Jr., E., Reed, C.E., Ellis, E., Adkinson Jr., N.F., Yunginger, J.W. (Eds.), Allergy—Principles and Practice, vol. 2. Mosby, St. Louis, CV, pp. 891–929.

Tada, T., Ishizaka, K., 1970. Distribution of gamma E forming cells in lymphoid tissues of the human and monkey. Journal of Immunology 104, 377–387.

Thatte, U.M., Chhabria, S.C., Karandikar, S.M., Dahanukar, S.A., 1987. Protective effects of Indian medicinal plants against cyclophosphamide neutropenia. Journal of Postgraduate Medicine 33, 185–188.

Thatte, U.M., Dahanukar, S.A., 1988. Comparative study of immunomodulating activity of Indian medicinal plants, lithium carbonate and glucan, methods and findings. Experimental and Clinical Pharmacology 10, 639–644.

Thatte, U.M., Kulkarni, M.R., Dahanurkar, S.A., 1992. Immunotherapeutic modification of *E. coli* peritonitis and bacteremia by *Tinospora cordifolia*. Journal of Postgraduate Medicine 38, 13–15.

Thatte, U.M., Dahanukar, S.A., 1997. The rasayana concept: clues from immunomodulatory therapy. In: Upadhayaya, S.N. (Ed.), Immunomodulation. Narosa Publishing House, New Delhi, India, pp. 141–148.

Wakode, P.T., Joshi, P.L., Mahore, M.N., 1989. Efficacy of nasal cytology. Indian Journal of Otolaryngology 41, 138–140.