

Evaluation of Takzema Tablets and Ointment (Multi-Ingredient Ayurvedic Formulation) in the Management of Eczema

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ABSTRACT

Eczematous diseases affect more than 10% of the general population and 15-25% of all dermatological patients suffer from eczema. Children are more prone to the disease and a significant number of affected children continue to experience symptoms in their adulthood. Although a large number of drugs are used for treating eczema, there is either no scientific evidence to support their use or they have undesirable side effects. Therefore, there is a need to provide treatment options that are safe and effective. The present study was conducted to assess the efficacy and safety of one such multi-ingredient formulation, Taczema, in patients with mild to moderate eczema. This was an 8-week, open labeled study of Taczema tablets and ointment in 50 patients of either sex suffering from mild to moderate eczema. Patients received 2 Taczema tablets BID for 8 weeks and Taczema ointment to be applied over the affected area/s thrice daily. Efficacy was evaluated on the basis of parameters of modified eczema area sensitivity index (EASI) and physician's and patient's global evaluation at follow-up visits. Forty-seven patients completed the study with reduction in symptoms of eczema to varying degrees. At the end of 2nd, 4th and 8th week, mean score of erythema had a reduction of 12.7%, 37% and 55%, mean score of oozing had a fall of 6.3%, 17.7% and 17.7%, mean score of indurations had a fall of 4%, 19.33% and 19.33%, and mean score of pruritus had a fall of 6%, 31.33% and 44%, respectively from baseline. Global assessment by the physicians and patients indicated fair to good response to Taczema. This study confirms the efficacy and safety of Taczema Tablets and Taczema Ointment in Indian patients with mild to moderate eczema.

Key words: *Eczema, Taczema, multi-ingredient Ayurvedic formulation*

INTRODUCTION

Eczematous diseases are very common with an estimated prevalence of more than 10% in the general population. According to statistics, 15-25% of all dermatological patients suffer from eczema. Surveys have shown that the prevalence of eczema is increasing. Eczema is a common chronic or relapsing dermatitis characterized by intense pruritus. It

occurs primarily in infants and children with a personal or family history of atopy. Nine to 12% of all children are affected with the disease^{1,2} and 60 to 70% of those with mild to severe dermatitis continue to experience symptoms into adulthood.³ A significant number of patients who have outgrown the typical manifestations of this disease, develop irritant dermatitis, which may be chronic in nature and may also interfere with the ability to work, especially in wet conditions or those involving chemicals.⁴

Pruritus is one of the most common symptoms of eczema. The itch-scratch cycle increases the damage to the epidermal barrier, thereby increasing water loss and drying, which creates a suitable environment for skin pathogens to cause infection and flaring of symptoms. Despite the frequent use of antihistaminic drugs in the management of eczema, there is no conclusive clinical evidence to support this practice. In fact, recent studies have shown that histamine has no role to play in the pathogenesis of eczema pruritus. In the pathogenesis of eczema, the mast cells, which are associated with histamine release, produce mediators other than histamine (proinflammatory cytokines) and lead to pruritus. Thus, since histamine has no role to play in the pruritus associated with eczema, there appears to be no rationale for using antihistamines in eczema.⁵

It is believed that antihistaminic drugs primarily produce a sedating effect that helps in providing peaceful sleep. Since the intensity of the itch often increases at night, the sedative effect of these drugs might be useful. However, sedative effect during daytime is undesirable and may even be dangerous in hazardous work environments.

Therefore, there is a need to introduce treatment approaches that are effective and do not produce undesirable side-effects. Taczema (tablets and ointment) is one such Ayurvedic formulation that contains ingredients such as *Rubia cordifolia*, *Tinospora cordifolia*, *Berberis aristata*, *Azadirachta indica*, *Swertia chirata*, *Aloe barbadensis*, *Curcuma longa*, *Linum usitatissimum* and others. The objective of the present study was to assess the efficacy and safety of this formulation in patients with mild to moderate eczema.

MATERIALS AND METHODS

This was an open labeled study of Taczema tablets and ointment in 50 sequential patients of either sex between 18 to 55 years of age suffering from mild to moderate eczema. Patients who attended our OPD and were willing to participate and give written informed consent were enrolled in the study. Patients were followed-up for a period of 8 weeks. Necessary approval for the protocol was obtained from our Institutional Ethics Committee before initiation of the trial.

Ambulatory patients of both sexes freshly diagnosed as well as pre-existing patients (with a wash out interval of 2 weeks if on treatment) with eczema and clinical diagnosis of eczema in any location of the body were included. The patients had clinical symptoms associated with eczema such as itching, oozing and desquamation.

The exclusion criteria included patients with infected lesions, history of ischemic heart disease, pregnant and lactating women; patients receiving corticosteroid treatment;

patients with history of gastritis, peptic ulcer, bleeding ulcers; HIV, HBV and known allergic reaction to systemic/topical study drugs. Patients were required to be administered other concomitant medications such as antihypertensives and oral hypoglycemic agents at stable dosage for at least 1 month.

Patients could be withdrawn from the study at their own request or if they experienced intolerable adverse events, showed insufficient therapeutic effect, or needed deviations from the protocol at the discretion of the investigator. A thorough physical examination and necessary laboratory investigations, which included hemoglobin, CBC count, ESR, liver and kidney function tests were carried out before drug administration and after completion of treatment.

After confirmation of diagnosis, patients meeting the inclusion and exclusion criteria were included in the study and received 2 Takzema tablets BID for 8 weeks and Takzema Ointment to be applied over the affected area/s thrice daily as a thin film and rubbed in gently and completely for 8 weeks.

Safety and efficacy evaluation of patients' clinical response to treatment was monitored from screening (day 0) till the end of therapy (end of 8 weeks). All data were carefully entered in the Case Record Form provided. Side effects were closely monitored in all patients. All adverse events were recorded by the investigator, and rated for severity and relationship to the study medication. However, significant exacerbations or worsening of pre-existing conditions were recorded. Drop out cases with reasons (non-compliance, side-effects or others) were noted. Any abnormal laboratory values were also noted.

The efficacy was evaluated on the basis of parameters of modified eczema area sensitivity index (EASI), physicians and patients global evaluation at follow-up visits. EASI involved scoring each area for intensity of erythema, oozing/crusting, indurations and pruritus on a 0-3 scale (0 = none, 1 = slight, 2 = moderate and 3 = severe).

The investigator global assessment (IGA) on efficacy and tolerability was performed on a scale of 1-5, namely Very Good = 5, Good = 4, Fair = 3, Poor = 2 and Very Poor = 1. Patient's global assessment on the efficacy and tolerability of treatment was similarly performed.

Patients lost to follow-up or withdrawn from the study at any time, whether due to inadequate response or adverse events, was also considered as failure. The results were analyzed on an intention-to-treat basis. The t-test was used to compare the statistical significance of outcome over baseline at 95% confidence interval.

RESULTS

Of the 50 patients enrolled in the trial, 3 were lost to follow-up while 47 completed the study with reduction in symptoms of eczema to varying degrees.

The demographic characteristics of these are as given in Table 1.

Table 1

Demographic Characteristics of Patients		
Age (years)	Male	Female
18 – 29	8	5
30 – 39	9	9
40 – 49	4	4
Above 49	7	4
Sub total	28	22
Total	50	

Treatment with the Takzema tablets and Takzema ointment was well tolerated and did not lead to any abnormalities in the laboratory investigations as compared to the baseline values. Patients tolerated the trial medications without any major adverse events that needed discontinuation. However, a few patients did experience minor adverse effects, which are summarized in Table 2 below.

Table 2

Adverse Events	No. of Patients (n = 50)	(%)
Epigastric pain	1	2
Nausea	2	4
Vomiting	1	2
Headache	1	2
Total	5	10

Table 3 shows the changes in the mean score of erythema, oozing/crusting, indurations and pruritus. At the end of 2nd, 4th and 8th week, mean score of erythema had a reduction of 12.7%, 37% and 55%, respectively from baseline. At the end of 2nd, 4th and 8th week, mean score of oozing had a fall of 6.3%, 17.7% and 17.7%, respectively from baseline. At the end of 2nd, 4th and 8th week, mean score of indurations had a fall of 4%, 19.33% and 19.33%, respectively. At the end of 2nd, 4th and 8th week mean score of pruritus had a fall of 6%, 31.33% and 44% respectively from baseline.

Table 3

Symptoms	Changes in Mean Score ± SD			
	Baseline	Week 2	Week 4	Week 8
Erythema	1.70 ± 0.54	1.44 ± 0.54	1.00 ± 0.57	0.7 ± 0.76*
Oozing	1.40 ± 0.61	1.30 ± 0.50	1.10 ± 0.37	1.10 ± 0.42
Indurations	1.74 ± 0.72	1.62 ± 0.60	1.30 ± 0.54	1.30 ± 0.54
Pruritus	1.92 ± 0.75	1.74 ± 0.69	1.20 ± 0.76	0.94 ± 0.91*

*p<0.05

At the end of 8 weeks, intensity of individual parameters like erythema and pruritus showed a statistically significant improvement from the baseline ($P < 0.50$), while oozing and indurations also reduced (Pictures 1A, 1B, 2A, 2B, 3A and 3B).



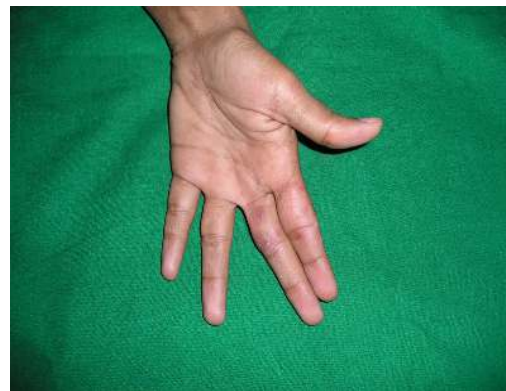
Picture 1A: Pre-treatment



Picture 1B: Post-treatment



Picture 2A: Pre-treatment



Picture 2B: Post-treatment



Picture 3A: Pre-treatment



Picture 3B: Post-treatment

The global assessment of response by physicians showed that 30% of patients showed a good improvement while another 52% showed fair improvement in their condition by the end of 8 weeks of treatment. Similarly, the patients' global assessment indicated fair to good response in 88% of the patients at the end of treatment.

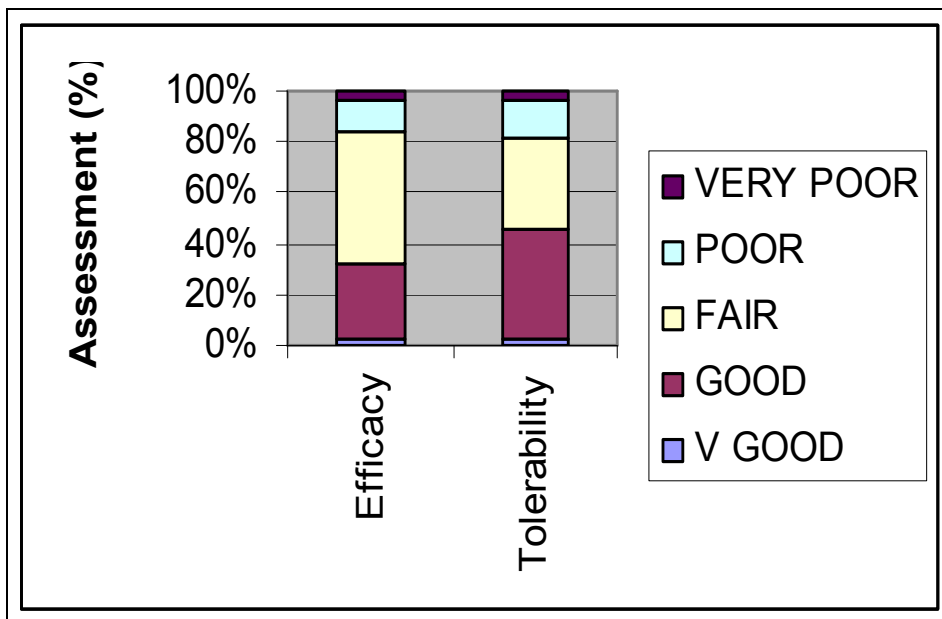


Figure I: Investigator Global Assessment (IGA) On Efficacy & Tolerability

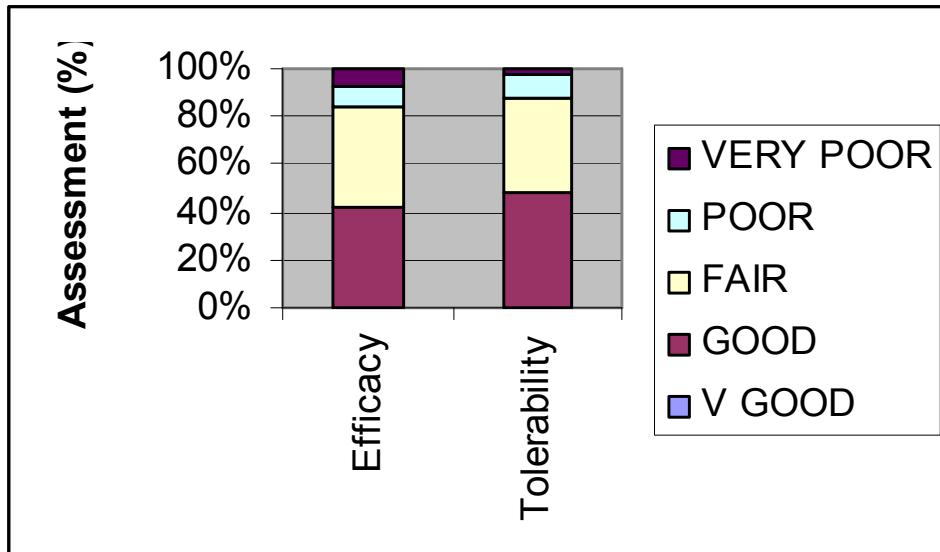


Figure II: Patients Global Assessment (IGA) On Efficacy & Tolerability

DISCUSSION

Eczema offers a wide clinical spectrum ranging from minor forms presented by a few dry eczematous patches to major forms with erythematous rash.⁶ The exact pathophysiological mechanisms leading to eczema are still elusive and various studies have tried to unravel the key factors leading to this disease.⁷ Nevertheless, continuing research on this disease has provided us with several insights into its pathophysiology. For example, it is now known that eczema is associated with an increased level of IgE (immunoglobulin E) in about 70-80% of the patients. IgE is an antibody subclass (known as "isotypes"), found only in mammals. Although IgE is typically the least abundant isotype, it is capable of triggering the most powerful immune reactions. Most of our knowledge of IgE has come from research into the mechanism of a form of allergy known as type 1 hypersensitivity.

The role of immune dysfunction and inflammatory mediators with respect to eczema has been a subject of intense inquiry. IgE-mediated hypersensitivity reactions are largely regulated by T-lymphocytes and it is generally accepted that the increased prevalence of eczema in recent years is due to a disturbed balance of Th1 cells and Th2 cells with a clear predominance of Th2 cells.⁸ The latter preferentially produce inflammatory mediators such as IL-4, IL-5, IL-10 and IL-13, which induce IgE production and activation of eosinophils, thereby producing typical features of allergic diseases.⁹

Disturbances in skin function are also a major etiological factor in eczema. The disease is characterized by intense pruritus and scratching in combination with cutaneous hyperreactivity and reduced threshold for pruritus. This forms a vicious circle of continuous mechanical stimulation and dysregulated cytokine release by keratinocytes. Further, the lipid composition of the stratum corneum of the epidermis is also damaged in eczema. This leads to dryness of the skin and a higher permeability to allergens and

irritants.¹⁰ Thus, eczema can be described as a primary, continuous defect of epidermal differentiation and functions in the presence of subclinical inflammation-induced skin damage in combination with a further impairment of the skin barrier during the active phase of the disease.

In addition to these insights, it is now also being realized that one important triggering factor of the disease is stress. Even though the exact mechanisms of the interaction of the skin immune system and the nervous system have not yet been identified, it is believed that this phenomenon might be mediated by neuroimmunological factors such as neuropeptides, which can be found within the epidermal nerve fibres in close association with epidermal Langerhans cells.¹¹

Considering this multifactorial etiology of eczema, it is only logical to expect an encouraging response in this trial to the herbal formulation Takzema. This formulation contains herbal ingredients that attack several pathological mechanisms discussed in the preceding paragraphs. For example, Leaves of *Azadirachta indica* and its constituents have been demonstrated to exhibit immunomodulatory, anti-inflammatory, antiulcer and antioxidant properties. *Phyllanthus emblica* helps protect the skin from the damaging effects of free radicals, non-radicals and transition metal-induced oxidative stress.^{12,13}

Curcuminoids from *Curcuma longa* have been demonstrated to protect normal human keratinocytes from hypoxanthine/xanthine oxidase injury.¹⁴ Plants such as *Rubia cordifolia*, *Glycyrrhiza glabra*, *Berberis aristata* and *Curcuma longa* have been used in Ayurveda for their wound healing properties (*Vranaropaka*). This property of these plants has been confirmed experimentally. Moreover, these herbs also show anti-inflammatory activity by suppressing reactive oxygen species and pro-inflammatory cytokines, the two important inflammatory mediators.^{15,16} Finally, *Tinospora cordifolia*, in addition to its well-known effect of regularising WBC function, also differentially regulates the elevation in cytokines.¹⁷

Thus, Takzema is useful in the management of eczema by enhancing the continuity of the epidermis through its protective and antioxidant functions. It also controls the inflammation-induced skin damage by inhibiting inflammatory cytokines. In addition, Takzema helps in countering the effects of stress and immune dysfunctions—factors which are now being recognized as important contributors to the etiology of eczema.

CONCLUSION

The current management of eczema revolves around the use of topical and systemic steroids, antihistamines and soothing and moisturizing agents. Use of steroids (topical and systemic) is fraught with side-effects. Antihistamines have practically very little to offer in eczema. Similarly, soothing and moisturizing agents can only offer temporary relief. In this situation, an Ayurvedic formulation like Takzema offers a promising alternative as it targets the pathophysiology of the disease, is effective and possesses an excellent safety profile.

In conclusion, this study confirms the efficacy and safety of Takzema Tablets and Takzema Ointment in Indian patients with mild to moderate eczema.

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