

A crossover double-blind study on *Tylophora indica* in the treatment of asthma and allergic rhinitis

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Results of a crossover double-blind trial on 110 bronchial asthma patients with leaves of Tylophora indica and of spinach (placebo) are presented. The dose was one leaf daily for 6 days to be chewed and swallowed early in the morning. A 12 week follow-up was done. At the end of one week, 62 per cent of the Tylophora group had complete to moderate relief in symptoms, as compared with 28 per cent of the placebo group. At 4 weeks, the respective figures were 37 per cent and 11 per cent; at 8 weeks, 30 per cent and 7.4 per cent; and at 12 weeks, 16 per cent and zero per cent. The incidence of side effects, such as sore mouth, loss of taste for salt, and/or morning nausea and vomiting was 53 per cent in the Tylophora group and 9 per cent in the placebo group. There appeared to be a correlation between the incidence of side effects and degree of improvement. After crossover at the end of one week, 50 per cent of the Tylophora group had complete to moderate relief as compared with 11 per cent of the placebo group. The authors are not aware of any other drug which, when administered in a small dose once a day for 6 days only, will suppress the symptoms of allergic rhinitis and/or asthma for 8 to 12 weeks in a significant number of patients. It is postulated that irritative effects of the juice of the Tylophora leaf on the mucous membranes of the mouth, tongue, and stomach somehow suppress or diminish the response of the nasobronchial tissue to an inhalant allergen through some reflex mechanism.

In an earlier paper¹ we have described *Tylophora indica* and the circumstances under which the senior author first became acquainted with its therapeutic properties. In the preliminary trial, even a small dose (chewing one

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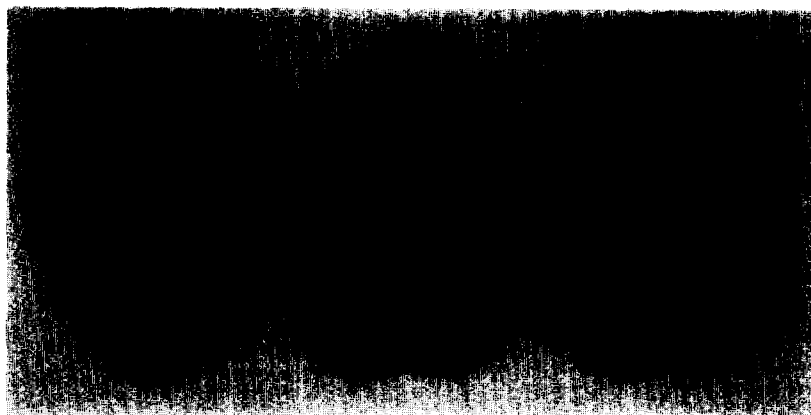


Fig. 1
Tylophora indica.

leaf of *Tylophora indica* daily on an empty stomach early in the morning) for 6 days had shown complete to moderate relief of symptoms lasting for several weeks in a good number of patients. The upper and lower aspects of the leaf are shown in Fig. 1.

As a natural sequel to the preliminary clinical trial, a crossover double-blind trial was planned. This article reports the results of the double-blind study.

METHODS AND MATERIALS

A total of 110 consecutive patients with bronchial asthma who were experiencing daily symptoms were taken into the trial and were allotted to Groups A and B by randomization. Care was taken to include only those patients who had symptoms daily and were known (from history of past illness) to develop these symptoms for several months or throughout the year.

The diagnosis of bronchial asthma was based on a history of recurrent paroxysmal attacks of dyspnea at rest relieved by epinephrine or ephedrine. It was confirmed by the presence of diffuse rhonchi during the attack and by the absence of any other simulating organic disease by clinical, laboratory, and radiologic examination. The overwhelming majority of these patients showed positive skin reactions to one or more common allergens such as pollens, house dust, fungal spores, etc. The distribution of the 110 asthmatic patients taking *Tylophora* or placebo leaves is shown in Table I.

Spinach leaves were used as placebo. These and the leaves of *Tylophora indica* were cut separately into small pieces by the nonmedical staff, put into polythene bags, and given code names of A or B by the statistician; these names were unknown to the physicians. Each patient was given one leaf daily for 6 days only. The patients of Group A received A leaf and patients of Group B received B leaf.

Many of the patients were admitted to the wards for a week and were examined twice a day. Those who were treated as outpatients were advised to

Table 1. *Distribution of 110 bronchial asthma patients taking Tylophora or placebo leaf*

<i>Age group (years)</i>	<i>On Tylophora</i>	<i>On placebo</i>
10 to 14	10	7
15 to 44	34	44
45 and over	9	6
Total patients	53	57

keep a daily diary for three things: (1) the frequency of symptoms; (2) the severity of symptoms; and (3) the amount of prescribed drugs which had to be taken to relieve those symptoms. They were required to visit the clinic every week for 12 weeks, with their diaries, for a full examination by the physician.

Methods of assessment

Assessment was done by the degree of freedom from symptoms and lung signs by repeated examinations. Notes were kept of the following points from day to day and week to week: (1) frequency of symptoms of wheezing or attacks of dyspnea; (2) severity of the symptoms, mild, moderate, or severe; (3) the amount of the prescribed drugs which had to be taken in 24 hours to relieve the symptoms; and (4) the presence and severity of lung signs, particularly rhonchi during normal and forced expiration.

The following drugs were prescribed and were to be taken in the following order: isoproterenol, 10 mg. sublingually; if there was no relief in 5 minutes, then one tablet containing ephedrine hydrochloride, 32 mg., aminophylline, 100 mg., and phenobarbital, 32 mg.; if there was still no relief in 30 minutes, then epinephrine hydrochloride (1:1,000), 0.5 ml. subcutaneously by drop method; if there was still no relief in 20 minutes, then aminophylline, 0.25 Gm., in 10 ml. of glucose slowly intravenously.

Definition of criteria of improvement²

The following clinical criteria of improvement were adopted: Complete: (100 per cent) no symptoms, no drugs used; Marked: (75 to 99 per cent) frequency of attacks reduced to less than one fourth and mild symptoms during the attacks; Moderate: (50 to 75 per cent) frequency of attacks reduced to less than half and moderate symptoms during attacks; Slight: (30 to 50 per cent) frequency of attacks reduced by more than one third and moderately severe symptoms during the attack; Nil: either frequency of attacks reduced by less than one third or no improvement at all.

In those who improved, the degree of improvement was assessed, and they were followed for the next 3 months with periodic examinations and assessment or until all signs of improvement were gone, whichever was earlier.

Crossover double-blind trial

Those who had no benefit from one type of leaf (Code A or B) or patients who experienced loss of improvement and the return of symptoms were given

Table II. *Results of first double-blind trial on 110 patients with bronchial asthma*

<i>Data</i>	<i>End of first week</i>	
Type of leaf	T	P
Number of patients followed	53	57
Degree of improvement (%) $\left\{ \begin{array}{l} 100 \\ > 75 \\ > 50 \end{array} \right.$	10 (18.9%) 15 (28.3%) 8 (15.1%)	8 (14%) 4 (7%) 4 (7%)
Total improvement over 50%	33 (62.3%)	16 (28%)

53 patients received one Tylophora leaf each day for 6 days only and 57 received placebo

T = Tylophora, P = placebo.

*N = None.

the second type of leaf (Code B or A) for another 6 days, and assessments were made as described previously.

At the end of the trial, the record of the assessment was handed over to the statistician. After the analysis of results was complete, he revealed the key which showed that A was spinach leaf and B was Tylophora leaf.

Pulmonary function tests (FEV and FEV₁) were performed in the majority of admitted patients before beginning the treatment, but, after their discharge from the wards after one week, these could not be repeated during the follow-up period, particularly in those patients who had shown marked clinical improvement. This happened because the pulmonary function laboratory is located in another building; when the patient visited us with his diary and was sent there after clinical examination, he was asked by the laboratory staff to come the next day or the day after, which he never did. To avoid this difficulty, we have now obtained a Wright's peak flowmeter and are presently using it in the clinic itself in a double-blind trial with an alcoholic extract of the Tylophora leaves.

RESULTS

Results of the first double-blind trial

The results are shown in Table II. Of the 53 patients in the Tylophora group, at the end of the first week, 62 per cent had moderate to complete relief in symptoms as compared with 28 per cent of the 57 patients of the placebo group. At the end of 4 weeks' follow-up, of the 49 patients of Tylophora group, 37 per cent still had complete to moderate relief of symptoms, as compared with 11 per cent of 56 patients of placebo group. At the end of 8 weeks' follow-up, of 47 patients of Tylophora group, 28 per cent still had complete to moderate relief of symptoms, as compared with 7.4 per cent of 54 patients of placebo group. At the end of 12 weeks' follow-up, of the 43 patients of Tylophora group, 16 per cent still maintained complete to moderate relief of symptoms, as compared with the zero per cent of 50 patients in placebo group.

Results of crossover double-blind trial

It will be noticed from Table III that, at the end of the first week, of the 48 patients who had placebo leaf in the first double-blind trial and then received

End of fourth week		End of eighth week		End of twelfth week	
T	P	T	P	T	P
49	56	47	54	43	50
10 (20.4%)	5 (8.9%)	7 (14.9%)	2 (3.7%)	4 (9.3%)	N
5 (10.2%)	1 (1.8%)	4 (8.6%)	2 (3.7%)	2 (4.6%)	N
3 (6.1%)	N*	2 (4.3%)	N	1 (2.3%)	N
18 (36.7%)	6 (10.7%)	13 (27.8%)	4 (7.4%)	7 (16.2%)	N

leaf in a similar way.

Tylophora leaf, 50 per cent had complete to moderate relief of symptoms, as compared with 11 per cent of 36 patients who had *Tylophora* leaf in the first double-blind trial and then received placebo leaf.

Side effects

It will be seen from Table IV that about 53 per cent of patients had side effects with *Tylophora* leaf as compared with 9 per cent with placebo leaf. The chief side effects were sore mouth, loss of taste for salt, and/or morning nausea and vomiting lasting for as many days as the leaf was used.

DISCUSSION

We do not claim that *Tylophora indica* cures asthma; but the results of this double-blind trial seem to indicate that even after a small dose of 6 leaves, at the end of one week there was complete to moderate degree of relief of symptoms of nasobronchial allergy in about 62 per cent of patients as compared with 28 per cent on the placebo leaf. This difference between the *Tylophora* and placebo groups became more marked during the follow-up, as seen from the results at 4, 8, and 12 weeks in Table II and the results of the cross-over double-blind trial in Table III. We do not know of any drug which, when given in such a small dose for 6 days only, will produce complete to moderate relief of symptoms lasting 8 to 12 weeks in a good percentage of cases.

The other important feature was that there was a high incidence of side effects with *Tylophora* leaves, i.e., about 53 per cent as compared with 9 per cent with placebo leaves. It will be noticed from Table IV that there appears to be some direct relationship between the incidence of side effects and the degree of relief in symptoms. It seems to us that irritative effects of the juice of the *Tylophora* leaf on the mucous membranes of the mouth, tongue, and stomach somehow suppress or diminish the response of the nasobronchial tissues to an inhalant allergen through some reflex mechanism.

The problem deserves further investigation. A double-blind trial with an alcoholic extract of the leaves of *Tylophora* and animal experiments to study its effects on the phenomenon of anaphylaxis are being carried out. The results will be reported in our next communication. However, our preliminary results from animal experiments in guinea pigs sensitized to egg albumin have shown

Table III. Results of crossover double-blind trial on 48 patients who received placebo leaf first and then *Tylophora* leaf, compared with 36 patients who received *Tylophora* first and then placebo

Degree of improvement	End of first week			
	48 patients who crossed over to <i>Tylophora</i> leaf		36 patients who crossed over to placebo leaf	
	Number	%	Number	%
100%	12	25	—	—
> 75%	4	8.3	2	5.5
> 50%	8	16.6	2	5.5
> 50% total	24	50	4	11

Table IV. Incidence of side effects in relation to the degree of improvement with *Tylophora* leaf compared with the similar data with placebo leaf (at the end of one week)

Degree of improvement	Type of leaf used	Number of patients	Number of patients with side effects
100%	<i>Tylophora</i>	10	7 (70%)
	Placebo	8	—
> 75%	<i>Tylophora</i>	15	9 (60%)
	Placebo	4	1
> 50%	<i>Tylophora</i>	8	4 (50%)
	Placebo	4	—
> 33%	<i>Tylophora</i>	6	3 (50%)
	Placebo	2	1
< 33%	<i>Tylophora</i>	14	5 (35.7%)
	Placebo	39	3 (7.6%)
Total	<i>Tylophora</i>	53	28 (52.6%)
	Placebo	57	5 (8.7%)

that parenteral or oral administration of aqueous or alcoholic extracts of *Tylophora* leaves does not protect them from anaphylactic shock produced by intravenous challenge.

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