Results of an open clinical trial with FH84 (Cernitin Pollen Extract) in patients with Pollinosis

Mazzi Rodolfo, Lugano, Switzerland (1986).

Aim of the trial

To evaluate the effect of FH84 in patients, who are allergic to flower pollen and suffering from pollinosis. The trial should provide information on the improvement concerning the symptoms (mainly Rhinitis and Conjunctivitis) and on the occurrence of adverse (allergic) reactions. The patients have been treated in 4 centers.

Principal Investigator	Dr. R. Mazzi, Locarno, CH	Centre 1
Co- Investigators	Dr. G. Bolognini, Mendrisio, CH	Center 2
	Dr. S. Gilardi, Locarno, CH	Center 3
	Dr. T. Pani, Lugano, CH	Center 4
Sponsors	Cernitin SA, Lugano, CH Lagap SA, Lugano, CH	
Dosage	1-2 sachets of FH84/day corresponding to 840mg T60 and 42mg GBX/sachet (1 sachet = 3g)	
Period of treatment	March - July 1985 and 1986 respectively	

Summary

FH84 taken prophylactic ally in early spring has caused a positive respond in 66% of a collective of 45 patients suffering from pollinosis. The patients have reported of an improvement of symptoms, especially concerning Rhinitis, Conjunctivitis and Sneeze. Age and sex of the patients did not significantly influence the result of the treatment. The date of start of treatment, whether March or April did not influence the results. There seemed to be a clear dose/response relation. Patients treated with 2 sachets per day form by far the best group with only “good” or “completely disappeared” results. No adverse reactions have been observed. Even a high dosage of FH84 (up to 1.6 gram of Cernitin Pollen Extract) administered per os did not cause allergies patients usually highly allergic to flower pollen.

Introduction

FH 84 contains as active ingredient a flower pollen extract, which is standardized in composition and production process (called: Cernitin Pollen Extract). During the spring of 1985 and 1986 respectively, 45 patients suffering from Pollinosis have been treated with FH84 prophylactic ally to evaluate the effect of the drug on the symptoms of Pollinosis. An additional aim of the trial has been to evaluate the tolerability of the Cernitin Pollen Extract, given per os at a high dosage to patients, known to be allergic against flower pollen.

FH84 is presented in powder form in aluminum sachets and has been administered daily per os (1 or 2 sachets). Each sachet contains 3g of FH84, which corresponds to 882 mg of Cernitin Extract {T60 (water-soluble components): 840 mg; GBX (fat-soluble components): 42 mg}.

The patients have been treated in 4 centers in Lugano and Locarno in the southern part of Switzerland. The trial has been carried out as an open trial. For each patient a detailed Case Record Form has been worked out and completed by the investigator(s).

Centers and Patients

The following 4 physicians participated in the trial:

Center 1: Dr. R. Mazzi, Locarno (CH) (Principal Investigator)
Center 2: Dr. G. Bolognini, Mendrisio (CH)
Center 3: Dr. S. Gilardi, Locarno (CH)
Center 4: Dr. T. Pani, Lugano (CH)

The patients have been divided as follows:

Table 1: Distribution of patients according to centers, sex and age.

	Center	1	2	3	4	Total
	Number of patients	22	13	5	5	45
Sex:	**Men**	10	9	3	4	26
	Women	12	4	2	1	19
Age:	**Under 25**	7*	5	2	3	17
	Over 25	7*	8	3	2	20

* for 8 patients of center 1 (1985) data on age are missing

Dosage

The normal dosage has been 1 sachet of FH84 per day. In center 2 however, 7 patients out of 13 have been treated with a double dose of 2 sachets daily.

Results

The results of the treatment have been evaluated in two ways:

a) Effect of the treatment on the following of pollinosis:
- Pruritis
- Sneeze
- Rhinitis
- Conjunctivitis
- Asthma

The patient had to report on each symptom whether at the end of the treatment it has:
- completely disappeared
- much improvement
- moderately improved
- remained unchanged
- deteriorated

b) General assessment of the treatment:
the patient and the physician had to judge each one separately, whether the result of the treatment has been considered as
- very good
- good
- mediocre
- non-satisfactory

4.1 Effect of FH84 on the symptoms of pollinosis

Table 2: Combined results 1985/86, 45 patients (figures are number of patients)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared	4	7	4	7	4
much improved	3	11	16	12	4
moderately improved	5	9	10	9	6
unchanged	6	11	13	11	6
deteriorated	1				

A majority of patients reported moderate to substantial improvement for the symptoms of Sneeze, Rhinitis and Conjunctivitis. 66,6% of the patients reported a positive response for Rhinitis, 62,2% for Conjunctivitis and 60% for Sneeze. Much improved

and/or completely disappeared were: 44,4% for Rhinitis, 42,2% for Conjunctivitis and 40% for Sneeze. Detailed data for each center are found in table 1-8 of the annex of this report. Even though the figures suggest quite a positive result for FH84, one has to consider the high placebo effect, the low number of patients and lack of statistical evaluation.

4.2 General Assessment of the treatment

Data on each patient concerning age, sex, dosage, start and end of the treatment, as well as concerning the assessment of the treatment are found in table 10-13 of the annex to this report.
The combined results of all 4 centers are shown in the following table:

Table 3: Combined results of the treatment of FH84, 1985/86, 45 patients

Centers	**1**	**2**	**3**	**4**	**Total**	**%**
Results						
very good	2	1	-	3	6	13.3
good	8	9	-	1	18	40.0
mediocre	5	1	-	1	7	15.6
non-satisfactory	7	2	5	-	14	31.1
adverse effects	0	0	0	0	0	0

68.9% of the patients responded positively to the drug. Good to very good response has been achieved by 53.3%. Over 15% showed a mediocre result and 31.1% did not respond at all.

4.3 Adverse Reactions to FH84

It is remarkable to notice that no adverse reactions (allergies) have been observed or reported due to the treatment with Cernitin Pollen Extract. One has to recall the high dosage of Pollen Extract in FH84 (corresponding to more than 10 tablets Cernilton/day) and the sensitivity of the special selected patients, who are generally allergic to flower pollen. From the present trial can be concluded, that per os intake of Cernilton Extract up to 882 mg/day do not cause any allergic reactions. 7 patients of center 2 have been treated with 1764 mg/day and did not show adverse reactions.

4.4 Effect of the treatment in function of the genus

The following table shows that there is no substantial difference concerning the sex, except that the assessment of “very good” is rarer in the groups of women.

Table 5:

	Number of Patients		**% of patients**	
	M	**F**	**M**	**F**
Total of patients	26	19	100	100
Results:				
Very good	5	1	19.2	5.3
Good	10	8	38.5	42.1
Mediocre	4	3	15.4	15.8
Non satisfactory	7	7	26.9	36.8

4.5 Effect of treatment in function of age

Table 6:

	Number of patients		**% of patients**	
	Under 25	**Over 25**	**Under 25**	**Over 25**
Total of patients	17	20	100	100
Results:				
Very good	3	2	17.6	10.0
Good	6	9	35.4	45.0
Mediocre	4	1	23.5	5.0
Non satisfactory	4	8	23.5	40.0

The only surprising difference is in the “mediocre” group, where under 25 years of age there is a percentage of 23.5%, but over 25 years only 5%. It seems that many of the over 25 years patients simply judge a mediocre result as “non satisfactory”.

4.6 Effect of treatment in function of dosage

The results of center 2 (see table 11 of annex) clearly show a much more consistent and better result by taking 2 sachets instead of 1 per day. All 7 patients report well to very good results. Such a result has not been observed in any other group or center.

4.7 Start/end of treatment

The date of start or duration of the treatment did not influence the results.

5. Conclusions

5.1 Efficacy

The prophylactic intake of FH84 in spring has caused a certain relief in the symptoms of patients suffering from pollinosis. Over 65% of the 45 patients reported of an improvement of their conditions at the end of the treatment, especially concerning the symptoms of Rhinitis, Conjunctivitis and Sneeze.

In this preliminary, open study no difference has been observed regarding sex and age of the patients. Also, the beginning of the treatment, whether March or April, seemed not to have any influence on the results. However, a treatment with a double dose (2 sachets/day) definitely improved the outcome of the treatment. The present results have not been statistically analyzed. One has to take into consideration the low number of patients and the high placebo effects, as well as the varying weather conditions. A final conclusion concerning the efficacy of the product will need a further trial with more patients and a control group ideally the trail should be blinded.

5.2 Tolerability

The present study is however very convincing concerning the tolerability of FH84. At the high dosage of 882 mg of Cernitin Flower Pollen Extract there has not been observed any adverse effects, say allergies in all 38 patients receiving this dosage. Seven patients receiving 1764 mg daily did also not show any allergic reaction. Thus, the conclusion is justified, that Cernitin Pollen Extract (FH84) does not cause allergenicity when administered orally.

ANNEX
Mazzi Rodolfo
Results of an open clinical trial with FH84
(Cernitin Pollen Extract)
in patients with Pollinosis (1986)

1. Data on single patients and evaluation of the therapy for each patient
2. Effect of FH84 on the symptoms
   (Pruritis, Sneeze, Rhinitis, Conjunctivitis and Asthma)
   Table 1-9

Dr. R. Mazzi, Center 1

Patient Number	Initials	Sex	Age	Dosage (Sachets/d)	Start	End	Adverse Reactions	RESULTS very good	RESULTS good	RESULTS mediocre	RESULTS non-satisfactory
1985											
1	P.F.	M	-	1	01.06.	01.07.	none	X			
2	C.A.	M	-	1	15.03.	01.07.	stomach		X		
3	A.R.	M	-	1	15.03.	01.07.	none	-*	-*	-*	-*
4	L.G.	M	-	1	15.03.	01.07.	none			X	
5	G.N.	F	-	1	15.04.	15.06.	none		X		
6	A.M.	M	-	1	15.01.	15.06.	none			X	
7	Z.G.	F	-	1	01.05.	31.05.	none		X		
8	A.A.	F	-	1	01.05.	15.06.	none				X
9	P.P.	F	-	1	01.05.	15.06.	none				X
1986											
1	P.E.	F	47	1	20.03.	03.08.	none				X
2	C.N.	M	16	1	20.03.	03.08.	none			X	
3	D.M.	F	19	1	18.03.	30.05.	none				X
4	P.G.	F	42	1	01.04.	26.07.	none			X	
5	A.R.	M	21	1	01.04.	15.06.	none	X			
6	K.D.	M	21	1	15.03.	15.04.	none	(X)	X		
7	B.Q.	M	40	1	01.04.	16.06.	none				X
8	S.C.	F	46	1	02.04.	16.06.	none		X		
9	I.R.	F	45	1	01.04.	04.06.	none				X
10	W.S.	F	26	1	30.04.	31.07.	none		X		
11	M.M.	F	15	1	08.04.	29.06.	none			X	
12	Z.G.	F	43	1	01.03.	30.06.	none	(X)	X		
13	D.G.C.	M	20	1	08.04.	08.07.	none		X		
14	E.U.	M	20	1	15.04.	15.06.	ECZ. ?**				X

* results not recorded (eliminated from final evaluation)

** irritation of pre-existing eczema (hands); objectively doubtful.

Dr. G. Bolognini, Center 2

Number	Initials	Sex	Age	Dosage (Sachets/d)	Start	End	Adverse Reactions	RESULTS very good	RESULTS good	RESULTS mediocre	RESULTS non-satisfactory
1985											
1	C.M.	M	24	1	26.03.	03.05.	none		X		
2	G.P.	M	38	1	01.03.	30.05.	none				X
3	C.N.	F	41	1	28.02.	30.05.	none		X		
4	S.E.	M	42	1	04.03.	30.05.	none		X		
5	M.L.	M	35	1	23.03.	30.05.	none				X
6	B.M.	F	19	1	26.03.	19.06.	none			X	
1986											
1	N.B.	M	48	2	01.03.	31.05.	none		X		
2	C.N.	F	42	2	15.03.	15.06.	none		X		
3	V.G.	M	22	2	15.03.	15.07.	none	X			
4	B.M.	M	38	2	01.02.	01.06.	none		X		
5	B.M.	F	20	2	15.03.	30.05.	none		X		
6	M.A.	M	27	2	15.03.	30.06.	none		X		
7	C.M.	M	24	2	14.03.	30.06.	none		X		

Dr. S. Gilardi, Center 3

Patient Numbers	Initials	Sex	Age	Dosage (Sachets/d)	Start	End	Adverse Reactions	RESULTS very good	RESULTS good	RESULTS mediocre	RESULTS non-satisfactory
1986											
1	B.S.	M	34	1	29.03.	19.06.	none				X
2	S.J.	F	37	1	15.05.	05.07.	none				X
3	B.E.	M	47	1	15.04.	20.08.	none				X
4	B.B.	F	16	1	07.04.	20.08.	none				X
5	C.G.	M	16	1	15.04.	28.08.	none				X

Dr. T. Pani, Center 4

Patient Numbers	Initials	Sex	Age	Dosage (Sachets/d)	Start	End	Adverse Reactions	RESULTS very good	RESULTS good	RESULTS mediocre	RESULTS non-satisfactory
1986											
1	L.F.	M	30	1	24.02.	22.04.	none	X			
2	N.G.	F	54	1	13.03.	30.04.	none	X			
3	S.M.	M	20	1 (1.5.:2)	01.04.	23.05.	none			X	
4	S.L.	M	17	1	14.04.	30.05.	none		X		
5	M.S.	M	16	1	15.04.	13.05.	none	X			

Table 1: Results of Center 1, 1985, 8 patients (Dr. R. Mazzi)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared			1	1	
much improved		2	1	1	
moderately improved		3	3	2	1
unchanged		2	2	1	1
deteriorated					

Table 2: Results of Center 1, 1986, 14 patients (Dr. R. Mazzi)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared	3			2	2
much improved	1	5	5	2	1
moderately improved	4	5	3	4	
unchanged	1	4	5	5	1
deteriorated	1				

Table 3: Combined results of Center 1, 1985 and 1986, 22 patients (Dr. R. Mazzi)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared	3		1	3	2
much improved	1	7	6	3	1
moderately improved	4	8	6	6	1
unchanged	1	6	7	6	2
deteriorated					

Table 4: Results of Center 2, 1985, 6 patients (Dr. G. Bolognini)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared					1
much improved			3	3	1
moderately improved			1	1	1
unchanged			2	2	
deteriorated					

Table 5: Results of Center 2, 1986, 7 patients (Dr. G. Bolognini)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared		2			
much improved	1	4	5	5	2
moderately improved		1	2	2	4
unchanged					
deteriorated					

Table 6: Combined results of Center 2, 1985 and 1986, 13 patients (Dr. G. Bolognini)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared		2			1
much improved	1	4	8	8	3
moderately improved		1	3	3	5
unchanged			2	2	
deteriorated					

Table 7: Results of Center 3, 1986, 5 patients (Dr. S. Gilardi)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared		1	1		
much improved					
moderately improved					
unchanged	5	4	4	3	4
deteriorated					

Table 8: Results of Center 4, 1986, 5 patients (Dr. T. Pani)

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared	1	4	2	4	1
much improved	1		2	1	
moderately improved	1		1		
unchanged		1			
deteriorated					

Table 9: Combined results of all 4 Centers 1985 and 1986, 45 patients

	Pruritis	Sneeze	Rhinitis	Conjunct.	Asthma
completely disappeared	4	7	4	7	4
much improved	3	11	16	12	4
moderately improved	5	9	10	9	6
unchanged	6	11	13	11	6
deteriorated	1				

Results.

% Inhibition (=100-(inhibit/uninhibit) x100)

Konc.	T60, ZB 207	T60, ZB 208
5 mg/ml	0	4,5
5 x 10^{-1} mg/ml	0	0
5 x 10^{-2} mg/ml	5,5	3,2
5 x 10^{-3} mg/ml	0,7	0
5 x 10^{-4} mg/ml	7,2	0,2
5 x 10^{-5} mg/ml	2,3	12,5

Timothy	Conc.
94,1	100.000 SQ/ml
90,1	10.000 SQ/ml
76,8	1000S Q/ml
0	100 SQ/ml
0	10 SQ/ml
0	1 SQ/ml

(Encl. 1)

Conclusion

Using the Maxi-RAST inhibition system it is shown, that neither of the two extracts were able to inhibit the response of the patient 50% or more, which is the criterion for a positive response. Inhibition below 20% is considered an unspecific reaction.