

Alocado™

**Effect of Alocado™ complex treatment on PASI scores
on psoriasis patients**

Prospective Clinical Study

**Final report
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Introduction

Kedo Eurocosmetics Ltd. and Spider Pharm Industries Ltd. entered an agreement in September 2006, to test the Alocado™ product line on volunteers suffering from psoriasis as requested by Teva Pharmaceuticals Ltd. Hungary. This document contains the test results, which are available for anyone wishing to be informed about the products. Our aim is to address physicians, specialists (dermatologists), pharmacists and patients all at the same time.

1. About Psoriasis:

Psoriasis is a classic and common dermatological condition. It is defined as follows: an “inflammatory skin condition with increased epithelial proliferation, characterized by infiltrated plaques and silvery scaling”. According to international statistics 2-3% of the overall populations are affected by this condition in varying degrees.

In Hungary, the estimated number of patients lies between 200,000 and 300,000, although much fewer visit their physicians, because part of them has already lost faith in receiving effective treatment; the other reason for not seeing a physician is that they are in remission and do not see its importance. The causes of psoriasis are still unclear, but research has significantly advanced our understanding concerning the inflammatory process and the immunological background of the illness.

The cause of this condition is believed to be genetic in nature. The condition is characterized by an increased sensitivity of the skin, reacting to external and internal stimuli. These stimuli are the so-called “provoking factors.” The most important provoking factors are mechanical (injury or irritation of the skin), immunological, metabolic stimuli, and provocation by medicine and stress. A characteristic feature of the illness is the deterioration of quality of life. This is not a life-threatening illness, and its gravity is determined not by the physician, but the patient. This condition influences the patient’s everyday life as well as their social and working activities. Deterioration of the quality of life due to psoriasis can be as serious as that caused by heart disease or depression.

Clinically speaking, it is the most versatile skin disease. The most often affected parts of the body are: the scalp, the knees, the elbow, the buttocks, the genitalia, the navel, the flexures and the nails. Its most frequent forms: thick, silvery plaque, extensive, inflammatory plaque, tiny, punctiform lesions and incidental small blisters. From a medical point of view, the degrees of illness can range from an asymptomatic state through mild symptoms, with isolated plaques to persistent, thick plaques; from a gradual spread, to a degree, when joints are also affected and the complete surface of the skin is covered by erythroderma.

According to Prof. Christopher Griffith, the gravity of the illness depends on the degree of deterioration of quality of life, the resistance to therapy and the degree lesion spreading.

Seeing as psoriasis is an illness that influences the quality of life and its gravity is determined by the patient, the physician compares his or her own findings with the evaluation of the patient and offers the patient all available therapeutic alternatives. Finally, they will be able to mutually choose the best one. The therapy can be either local or system ic.

Local treatment consists of two phases: the first is stopping acute symptoms, and the second is maintaining therapy with the aim of avoiding a relapse. As for the medication used in

maintenance therapy it is of utmost importance that they be well tolerated by the patient, without any side effects.

There are very few preparations used so far, that comply with the above requirements. Traditional treatment possibilities for the acute phase are: coal tar, local corticosteroids, vitamin D analogues, local retinoids, and keratolytic agents (compounds containing salicylic acid, for external application). Besides these, Photo-therapy (PUVA, UVB) and bath therapy may also be applied.

1. The above therapies are effective, but they have several side effects:
2. Corticosteroids can cause atrophy of the skin; vasodilation may occur fungal or bacterial infections may emerge.
3. Vitamin D may be irritating and expensive.
4. The application of coal tar and some of the photo-therapies in large doses are carcinogenic.
5. Salicylic acid in high concentrations is irritating.

From the list of above-mentioned therapies only vitamin D is suitable for maintenance therapy. So the need for a phase-specific, non-aggressive (non-irritating) maintenance therapy is justified.

2. About Alocado™ treatment

The Alocado™ product line was developed in 1988 based on formulas developed by physicians and pharmacists working in clinics near the Dead Sea. At that time, it was recognized that the surroundings, the water and the mud of the Dead Sea had a healing effect on the patients suffering from skin diseases. This was also the time when some publications on side effects and disadvantageous features of steroids appeared. Sea minerals are Nature's ultimate supplement for maintaining healthy skin. The minerals essential to well-functioning skin – magnesium, calcium, potassium and sodium – naturally attract and retain water and are known as Natural Moisturizing Factors (NMF). As a person matures, the NMF levels of the body gradually become depleted, lessening the body's ability to retain the proper moisture levels needed to prevent skin aging. Urban pollution, the ongoing exposure to the elements and the fast-paced lifestyles we live, all take their toll. Dead Sea mineral formulae help to reactivate the skin's natural ability to hydrate and replenish itself and restore its natural suppleness. Realizing these facts, the inventors were inspired to develop a range of products solving all varying problems using a phase specific range of products that was a revolutionary departure from the "all in one" existing medicines. During their work, they could make use of some publications analyzing therapeutic effects of some vegetable oils like Avocado oil, and the Aloe Vera extract. Besides this, patients wished to enjoy remission not only for a week for as long as their treatment at the Dead Sea lasted, but for a longer period of time. This was made possible by being able to take these natural remedies back home.

Advantages of the Alocado™ product line are as follows:

1. It does not contain steroids.
2. It does not contain tar.
3. It does not contain synthetic vitamin D.
4. The acid content never exceeds 2%.
5. The active ingredients are combined with very strong emollients.

6. A unique composition of natural oils (mainly Avocado), Aloe Vera extract and salt from the Dead Sea (not reaching salt concentration levels that could irritate skin).
7. There are special products to treat different symptoms, including open wounds.
8. We offer products for maintenance therapy to be used in state of remission to contribute to palliate symptoms of the next relapse.
9. These products don't have side effects neither after short- nor after long-term treatment..

Study design:

1. Psoriasis study group:

1. Gender: 209 volunteers' women and men as equal.
2. Age: 18-75 years old
3. Health conditions: stable psoriasis at least last 12 months, PASI >2, body or/and head are affected.
4. Background: varied
5. Duration:
September 2006-September 2007
6. Termination:
After 3 weeks of the treatment.
7. Report:
Each doctor was follow-up his patient weekly and giving the PASI score that was documented in personal file of each patient. The mean PASI score was calculated for each patient and presented in the final report.
8. Treatment:
The follow Alocado™ products were used in the current clinical study:

<u>Product name</u>
Alocado™ Cream
Alocado™ Ointment
Alocado™ Pasta
Alocado™ Gold
Alocado™ Skin Softener
Alocado™ Silver
Alocado™ Bath Oil
Alocado™ Body Oil
Alocado™ Lotion
Alocado™ Scalp Oil
Alocado™ Zi-Con
Alocado™ Zal-Con
Alocado™ Shampoo
Alocado™ Hair Conditioner

We began testing Alocado™ products in September 2006. It was an open clinical prospective study over a period of one year. 208 volunteers were recruited to take part in the test, which was not launched at the most favorable period, because psoriasis generally relapses when cold weather is to be expected. Baseline data were collected along with the dermatological examination, i.e. personal data, medical history, and all medications taken before and at the time of this examination were recorded. The state of the skin was photographed. The exclusion criteria were unstable psoriasis, children, pregnancy, lactation, history of any thyroid disorder and severe systemic illnesses. The patients were assessed at the end of 2 and 3 weeks by 55 Dermatologists; each doctor treated and follow-up five volunteers. The volunteers were self-treated by different combination of the Alocado™ products daily and according to the instruction of the Dermatologist. Once a week, the volunteers were checked by the same doctor and the effect of the treatment was evaluated using PASI index. The PASI index widely accepted in specialist literature to establish condition changes.

We established values on the basis of PASI index from the starting state of illness, and during the repeated follow-ups.

A short summary on PASI:

The objective skin condition of the patient is expressed by the so called PASI index. This is an internationally accepted index to demonstrate the state of the skin and to establish efficacy of the therapy. The index evaluates the main symptoms of psoriasis: erythema, induration, and scaling, and the size of the affected area are taken into consideration as well. All these factors are taken into account in the regions of the head, the upper limbs, the torso and the lower limbs. Using different multipliers a relative number is achieved from the sum of these values. This relative number is not quite perfect; e.g. changing from PASI 20 to PASI 10 is much easier than to change from 10 to 5. There is a version of this index where the patients analyze the values themselves. (This happened in our case, when we had weekly or bi-weekly phone consultations with the patients.)

Since psoriasis is an illness influencing the quality of life, it is the patient who evaluates the illness most precisely; his or her opinion is crucial. The results are expressed as mean \pm SD. Student's unpaired t-test was used for statistical analysis of the data. Level of significance was $P < 0.005$.

The objective

The objective of our study was to assess the clinical efficacy of Alocado™ complex treatment in psoriasis.

Administering Alocado™ products, our aim was to give emollient, nourishing and calming preparations to the patient. These products are phase-specific, meaning that they always exert their effect against the most irritating symptom, and they support maintenance therapy in conjunction with drug therapy or without. The products prolong the period between relapses and make the patients feel more comfortable with their skin.

Results

When starting the Alocado™ treatment, we tried to choose patients who had not been treated with any steroids or other medicines within a given period before the test. However, taking these preparations was not a criterion for exclusion, since it is necessary to have some emollient treatment for those who took the aforementioned medication.

In any cases, improvement could be observed based on the regular application of the Alocado™ products. When stopping it, the skin's condition could deteriorate in some cases the conditions as it was before the treatment. We observed that the efficacy of the products, and the response to them could be increased by applying the appropriate Alocado™ product several times a day. It has been observed that application 4 times daily (this dosage proved to be necessary to achieve maximum efficacy) resulted in the fastest improvement.

Throughout the treatment, we had to change products with many patients, because Alocado™ products are phase-specific, and a different product is recommended depending on the predominant symptom (scaling, inflammation, infiltration). In patients showing improvement, the use of the compound called Gold should be emphasized, having a soothing effect on the itching, excoriated parts of the skin, which quickly epithelized and the patient soon became asymptomatic.

1. Three weeks after the treatment with Alocado™ complex all 208 patients showed significant improvement in their symptoms. The positive effect of the treatment was observed already after the first week of the treatment. The Table 1 summarized PASI index scores as per follow-up. As it can be seen in the table the positive effect of the treatment was achieved independently on the severity of the disease or on the affected area percent.

Patients		PASI		
Number	1 st week	2 nd week	3 rd week	
1	4		3.2	2.8
2	3		2.4	1.5
3	4.6		3.6	2.1
4	7.4		4.2	2.9
5	6.8		6	3.2
6	11.3		9.8	7.6
7	7.1		4.8	4.7
8	2.7		1.2	1
9	19.1		13.8	9.2
10	8.7		5.8	2.6
11	5.4		4.4	3
12	1.8		1.4	1
13	2.6		1	0.7
14	2.2		1.8	1.2
15	7.2		5.6	3
16	2.8		2.3	1.6
17	4.1		3.1	1.3
18	4.4		0.9	0.9
19	4.9		3	2.5
20	12.6		11.9	6.6

21	1	0.7	0.4
22	27	21	15
23	2.2	1.6	1.4
24	48	24	20
25	3.1	1.8	1.4
26	13.7	7.4	5.2
27	8.6	7.9	5.7
28	1	0.9	0.5
29	2.4	0.8	0.4
30	9.1	6.1	5.2
31	2	1.2	1
32	2.6	2.2	0.5
33	1.3	1	0.6
34	3.1	2.1	0.6
35	3	1.3	0.8
36	5.6	4.8	1.6
37	12	7	7
38	2.4	1.8	1.2
39	7.4	4.2	2.9
40	2.4	1.8	1.2
41	10.9	6.6	3.3
42	3.7	3.1	3
43	2	2	1.6
44	5.2	4	1.2
45	3.6	1.4	1
46	5.2	4	1.4
47	4	2.8	1
48	5.2	4	1.4
49	3.6	1.4	1
50	5.2	4	1.2
51	0.8	0.8	0.7
52	9.9	9	5.4
53	23.5	23.3	19.9
54	7.2	6	3.2
55	3.6	3	1.6
56	21.6	18	5.1
57	7.2	5.4	1.8
58	4.8	4	1.4
59	1.6	1.4	1
60	11.2	8.8	2.8
61	3.1	2.1	1.3
62	4.4	3.7	2.5
63	9.9	8	4.5
64	8.4	8.2	7.5
65	7.2	6.6	4
66	4	3.2	3.2
67	8.4	6.6	2.4
68	26.4	14.7	8.7
69	4	1.6	1.2
70	5.2	4	1
71			

72	8.8	7.2	3.4
73	5.4	4.6	3.4
74	4	3.6	1.2
75	3.6	1.4	1
76	5.6	3.3	2.5
77	2.6	2	0.7
78	2.9	2.5	1.7
79	2.2	1.8	1.2
80	5.4	4.8	3.6
81	3.3	3	2.1
82	4.4	3.6	1.4
83	1.8	1.6	1.2
84	4	3.2	2
85	2.5	2.2	1.5
86	4	3.6	3.2
87	2	2	1.6
88	0.7	0.7	0.5
89	7.8	6	2.4
90	2	1.6	1.4
91	13.2	5.6	2
92	4	2.8	1.2
93	2	1.8	1.4
94	1.8	1.6	1.2
95	1.8	1.4	0.8
96	1.8	1.6	1.4
97	4.7	4.1	2.5
98	3.5	2.8	2.4
99	9.9	8	5.5
100	5.2	2	1.4
101	1	0.8	0.7
102	2.7	2.2	1.9
103	4.4	3.6	1.2
104	5.6	4.5	3.1
105	2.2	1.8	1.2
106	5.4	4.5	1.8
107	2.4	2	1.4
108	4.8	3.6	1.4
109	4.8	3.6	2.8
110	2.9	2.1	1.5
111	5.1	4	3.4
112	2.2	1.6	1.2
113	9.6	7.6	3.6
114	4	1.5	1
115	11.9	7.8	2.5
116	2.2	1.6	0.5
117	9.7	8.1	4.3
118	7.8	6	1.5
119	9.4	5.7	2.8
120	11.2	4.7	3.5
121	15.5	8.9	6.2
122			

123	17.3	13	4.3
124	20.6	13.5	7.2
125	22.4	14.7	5.8
126	10.6	5.1	2.4
127	9.8	7.7	3.3
128	15.8	9.6	7.2
129	26.4	20.4	7.2
130	46.8	38.2	18.9
131	13	12.8	5.8
132	15.4	9	0.6
133	13.5	10.5	6
134	26.1	17.1	12.1
135	17.9	15.9	8.5
136	17.6	12.8	6.2
137	6	3.6	1.2
138	3.3	2.7	1
139	6.4	5.2	1.8
140	5.6	4	2
141	2.2	1.8	0.6
142	4	2.8	1.6
143	13.2	9.6	5.6
144	4.4	3.5	2.9
145	6.6	4.8	1.6
146	2.8	1.8	1.6
147	31.2	24.6	17.8
148			
	2.2	7.8	6.6
149	25.2	1.8	1.6
150	26.5	22.6	20
151	24.4	22.2	20
152	2.2	1.8	1.6
153	8.4	7.8	6.6
154	3.6	2.8	1
155	41	35.2	17.4
156	17	11.4	3.4
157	45	36.8	21.5
158	25.6	22.7	9.4
159	19.2	13.2	6.8
160	18.6	15	8.7
161	4.4	3.5	2.9
162	2	1.6	0.7
163	20.4	10.2	10.2
164	20.5	12.2	11.5
165	18	13.2	6.4
166	41	29.8	16.5
167	41.8	19.4	15.6
168	41.4	30.8	16.5
169	33	24	14.7
170	26	9.5	2.4
171	47.8	38.1	35.9
172			

173	41.5	33.7	33.4
174	35.3	21.9	24.8
175	43.8	26.2	27.1
176	8	6	3
177	9	6	3
178	24	7	3
179	42	16	5
180	24	8	6
181	9.3	6.5	3.1
182	7.6	4.4	3.1
183	7.8	7.2	3.9
184	20.1	9.5	4.7
185	7.5	3.6	3.6
186	11.4	5.9	2.9
187	7.8	4.2	2.6
188	1	0.5	0.5
189	2.4	1.8	0.4
190	23.2	12.9	4.8
191	41.1	27.9	16.9
192	26.1	11.3	2.8
193	19.4	5	4.5
194	44.2	26	14.8
195	49.5	28	17.8
196	23.6	19.5	13.6
197	28.3	25.1	18.6
198	47.3	38.4	28.9
199	25	19.6	10.8
200	33	15.8	11.8
201	24.3	10.7	4.6
202	27.4	9.4	3.6
203	18	18	8
204	14	13.2	5.3
205	16	16	12
206	18.2	17.5	13.9
207	22.2	16.5	14
208	38.8	36.6	26.8
209	7.2	7.2	5.6
210	3.9	0.6	0.6
211	18	15.6	12
212	2.5	1.6	1.6
213			

As it can be seen in Figure 1 the PASI was decreased by 28% after 2nd week of the treatment (72% compare to the PASI index before the treatment) and by 55% in the end of the 3 weeks of the treatment (45% compare to the PASI index before the treatment). These results demonstrating a high and very fast significant positive effect of the Alocado™ complex treatment (unpaired t- test p<0.001). Furthermore, this effect was more remarkable in the patients with moderate – severe psoriasis (PASI above 7). As it can be seen in the Figure 2 the PASI was decreased by 34% after 2nd week of the treatment (66% compare to the PASI

index before the treatment) and by **65%** in the end of the 3 weeks of the treatment (35% compare to the PASI index before the treatment) (unpaired t- test $p < 0.001$).

The most important was the fact that **no side effects** were reported during the period of the treatment and within half year later as well.

2. Besides the significant improving in the symptoms, in 107 patients was observed significant reducing in the percent of the affected area of the body, as can be seen in the Figure 3. After 1st week of the treatment with Alocado™ complex the percent of the affected area of the body was reduced by 8% as compare to the beginning of the treatment (32% versus 40%) and by 23% in the end of the 3 weeks of the treatment (17% versus 40%) (unpaired t- test $p < 0.001$).

Figure 1.

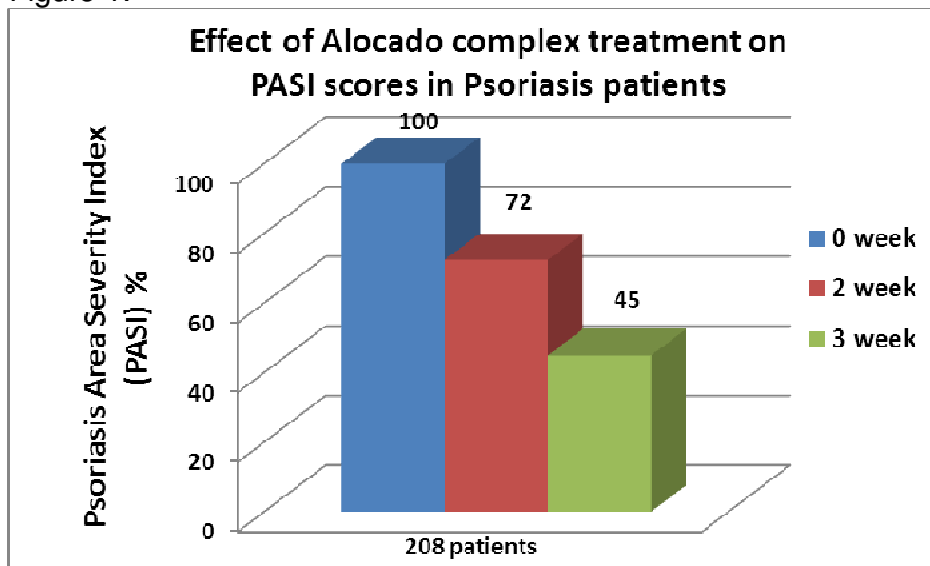


Figure 2.

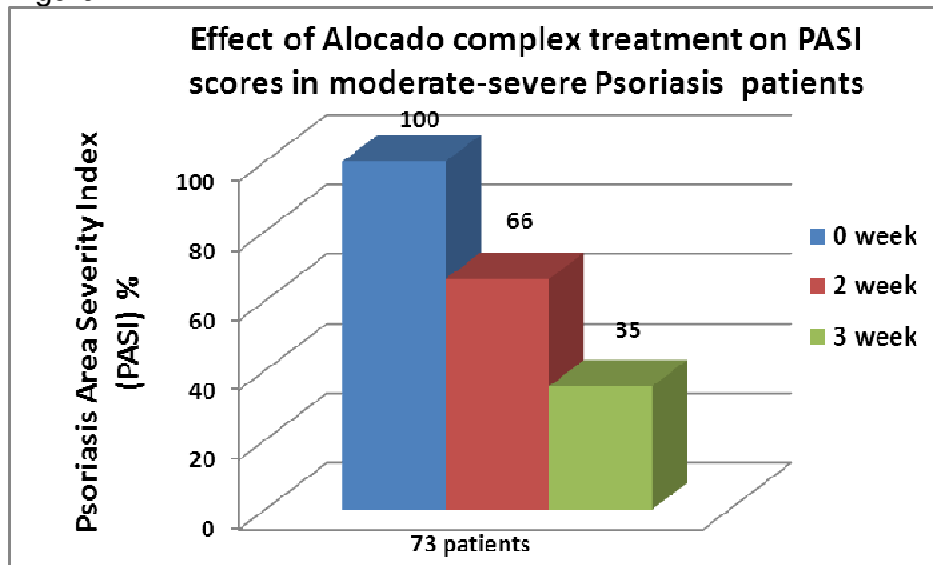
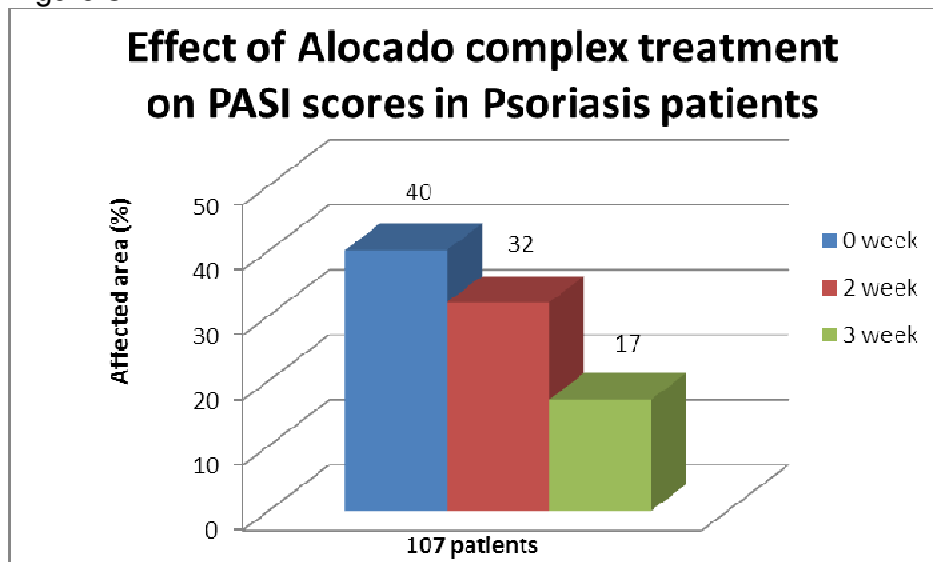


Figure 3.



Discussion

Psoriasis is a chronic inflammatory skin disease with a high social and psychological impact on the quality of life of patients. Literature reports that psoriasis can cause a physical and mental disability similar to other medical diseases, like hypertension and diabetes, and psychological distress can influence the rate of withdrawal during standard therapy, because patients who feel worse spend less time caring for their psoriasis.

The Dead Sea region is recognized worldwide for its efficacy in the treatment of dermatological diseases, particularly Psoriasis, Atopic Dermatitis, Vitiligo, and Mycosis Fungoides. Sea minerals are Nature's ultimate supplement for maintaining healthy skin. The minerals essential to well-functioning skin – magnesium, calcium, potassium and sodium – naturally attract and retain water and are known as Natural Moisturizing Factors (NMF). As a person matures, the NMF levels of the body gradually become depleted, lessening the body's ability to retain the proper moisture levels needed to prevent skin aging.

We conducted a prospective clinical trial on 208 patients affected by mild to severe psoriasis undergoing Alocado™ complex therapy. We recorded a significant reduction of the mean Psoriasis Area and Severity Index (PASI) index in all 208 patients who completed the three-week course and an improvement of the 'quality of life' of patients. In addition, the recurrence of the symptoms 6 months later without treatment that was observed in few cases was usually less severe than the previous attack. It should be mentioned that **no side effects** were observed. The good efficacy obtained by this treatment, and the psychological impact on the quality of life of patients, demonstrated that Alocado™ complex therapy could be a very good option for the treatment of a chronic disease associated with psychological distress, like psoriasis, particularly when the patient is affected by other diseases, and we cannot use any systemic psoriasis drug.

What is not less important that this treatment is more cost-effective than many other treatments.

Conclusion

Based on these results, it may be concluded that the phase-specific, emollient, palliative natural compounds of the ALOCADO™ product line offer a **highly effective, very fast and safe** alternative for the treatment of psoriasis.

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Appendix 1

I. ATOPIC DERMATITIS

Clinical test for ALOCADO™

- A woman of 29 years of age
- Suffering from Atopic Dermatitis for 12 years.
- Treated with all kinds of medicine, including injections and steroids.
- Past two years, no changes.
- Start of treatment 8.11.06 – before photo.
- Last check 31.12.06 – after photo.
- Treated with Alocado™ Cream and Alocado™ Skin Softener, to be applied three times a day, first Alocado™ Skin Softener and when absorbed, Alocado™ Cream. When itchy, Alocado™ Cream can be applied as much as needed.
- In 31.12.06 Alocado™ Gold was added to treat open wounds left on the body,
- 10.01.07 wounds are closed; most of the skin is clear, continue maintenance treatment with the Alocado™ Cream.

Before



After



II. PSORIASIS

Clinical test for ALOCADO™

- 75 years old
- PASI index at start 39.2 for the past 15 years no improvement whatever medicine taken.
- Very swollen, red and inflamed skin, sometimes very itchy, others not
- Some areas are covered with thin plaque.
- At current situation, using medicine with steroids, help minor.
- Started Alocado™ treatment at the 28/9/06 received Alocado™ Gold for treating inflammation and Alocado™ Pasta for treating red swollen skin.
- The moment stop taking medicines within one week situation worsen to 55 in PASI index (steroid effect).
- After 1 month when inflammation reduced, Alocado™ Body oil and Alocado™ Cream for itching and dry skin were added. So treatment included Alocado™ Gold, Alocado™ Body oil, Alocado™ Pasta and Alocado™ Cream, when inflammation was reduced to zero Alocado™ Gold was stopped. After 1 more month at the 3rd of December 2006 the PASI index dropped to 13.2.
- No Itching, No scaling, No inflammation, No swelling, No redness (small red dots are the only thing left, typical to old peoples skin), fingernails grew back better than before (were treated with Alocado™ Skin Softener).
- Over all, pretty satisfying results.
- Ongoing treatment – Alocado™ Cream, Alocado™ Body oil and Alocado™ Skin Softener for maintenance.



