Melatonin cream and melatonin-resveratrol LAA 15% serum and Quantum Molecular Resonance technology as ideal treatment for age related skin deseases

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Summary

Melatonin cream and melatonin-resveratrol LAA 15% serum and Quantum Molecular Resonance technology as ideal treatment for age related skin deseases

A new melatonin multivitamin complex in combination with the purest vitamin C [L-ascorbic acid (LAA)] stabilized with resveratrol and Vitis vinifera has been developed to topically treat sun damage, anti aging and actinic keratoses. The skin of sixty patients using a new revitalizing procedure based on Quantum Molecular Resonance (QMR) technology has been also used in order to value if and how skin face could improve with both treatments. The study was conducted over three years with 264 patients, ages ranging from 28 to 85 years old. The new melatonin multivitamin complex in combination with vitamin C 15% stabilized with melatonin, resveratrol and Vitis vinifera, improves the intrinsic aging and photo-aged skin. QMR technology improves significantly the results increasing the amount of collagen and ameliorating the skin texture.

KEY WORDS: *Skin aging, Melatonin-resveratrol LAA 15% serum, Quantum Molecular Resonance*


Matteo Tutino

Introduction

The signs and symptoms of aging affect several organ systems. The skin is our largest organ. It functions as a barrier, protecting the body (internal environment) from the external environment. Skin problems may be the first symptoms of aging and a window to internal organ deterioration. Skin is our first organ to show signs of sun damage.
We have developed a new melatonin multivitamin complex in combination with the purest vitamin C [L-ascorbic acid (LAA)] stabilized with resveratrol and *Vitis vinifera*, to topically treat sun damage, anti aging and actinic keratoses. We also treated the skin of sixty patients using a new revitalizing procedure based on Quantum Molecular Resonance (QMR) technology in order to value if and how skin face could improve with both treatments. Our study incorporated 264 patients over a three year period and took an objective view on how this new topical product treats the aforementioned skin changes.

Study design

The study was conducted over three years with 264 patients, ages ranging from 28 to 85 years old. We divided the patients into 2 groups: control and study.
The patients were selected randomly and based on their psychological examination, evaluation and clinical assessment. In addition, the study group received our treatment protocol and the

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control group used vitamin C serum and simple moisturizer. All patients were allowed to continue their normal cosmetic treatments (botox, fillers, etc). Actinic keratoses was included among the pathologies as it may represent the natural evolution of sun damaged skin or a chronologic aged skin when the mitochondrial DNA has already expressed mutation [1-4]. Those suffering from actinic keratoses in both the study and control group, received cryotherapy or radiofrequency.

Materials and Method

Melatonin has been used experimentally in skin function such as hair growth cycling, pigmentation and melanoma control. Melatonin receptors are present in several skin cells including normal and malignant keratinocytes, melanocytes, and fibroblasts.
Melatonin both suppresses ultraviolet rays (UV) that induce damage to skin cells and shows a strong antioxidant activity in UV exposed cells. Moreover, we recently uncovered activity in the skin of the biochemical processes involved in the sequential transformation of L-tryptophan to serotonin and melatonin [5-8].
A new cream formulation was developed mixing melatonin with a multivitamin complex and antioxidant derivative from the grape (resveratrol), in order to obtain a synergistic effect during the application and improve penetration of the substances through the skin barrier. The new creams were all based on a ph controlled system. Another formulation was based on melatonin, resveratrol and LAA which have important biological functions for skin and all cellular tissues as well as an antioxidant and an anti-inflammatory action. Moreover, they exert a noticeable action in the modulation of the immune response: by stimulating synthesis of collagen in fibroblasts of the human skin. LAA, in particular, plays a role in homeostasis of the connective tissue system of human cells. Furthermore, LAA increases the synthesis of proteins and collagen with anti-wrinkling effects. This process has a blocking action with respect to ferric ions, preventing skin damage due to excessive exposure to the sun [9-13].
The basic protocol used in our study was based on an acidic pH which enhanced the penetration and the action of the following compounds [14]:

1) A cleanser for acidification of the skin to ph 3.5.
2) Vitamin C serum 15% which has a strong penetration a ph 2.8.
3) Melatonin resveratrol multivitamin complex cream a ph 4.5.

The system required an application of the compounds twice/day. According to the skin condition, some patients were asked to double the application of products on the individual skin lesion in order to have a stronger action.
We added a special formulation of tretinoin at a concentration of 0.1%, stabilized in vitis vinifera and resveratrol, to increase the intracellular action especially for actinic keratoses.
The Control group (made up of 94 patients) was administered only topical vitamin C serum LAA and a custom made moisturizing cream containing petrolatum.

4) QMR technology (fifty patients were included in the study group of Photo-Ageing and ten patients in the study group of Intrinsic Ageing): we used Rexon-Age technology plus the above-mentioned products. QMR protocol we used: 8 treatments to the whole face (1 a week). Exposure time: 50 minutes each treatment, 80 (mj/cmq)/S, electrode code n. 4 (handle).

The clinical application was conducted during the last 3 years, and each patient was selected according to a specific criteria based on clinical observations. Our study was carried out on a qualitative evaluation of the results, particularly on macroscopic evaluations. Histological examinations were realized only for those patients showing precancerous lesions. In photo-aged skin and intrinsic ageing, the histology was avoided in order not to create any discomfort to the patients since the clinical data did not justify any biopsies. Furthermore, every patient went through a psychological evaluation before, during and after the treatment period. Tests were performed to evaluate the satisfaction of the patients. In order to do this a questionnaire was given. The following questions were asked:

1. Have you noticed any improvements in the areas of the body that were treated?
2. Do such improvements correspond to your expectations?
3. Express a value from 1 to 6, where 1 = not satisfied and 6 = very satisfied your perception of the improvement of the skin in relation to:
   - hyper pigmentation
   - wrinkles
   - scars

- acne
- reduction of secretion of the sebum
- compactness
- pore reduction
- hydration
- brightness/luminosity.

4. Express a value from 1 to 6, where 1 = not satisfied and 6 = very satisfied on the quality of the creams in comparison to:
   - ease of application
   - smell
   - penetration/absorption
5. What was your state of mind when you first approached the treatment?
6. Do you believe that you can have an active role in the results of the treatment?
7. How much and to what extent do you feel that changes and/or improvements in your physical appearance has had or will have influence in your interpersonal relationships?
8. How do you view a medical approach that focuses on both the physical and psychological aspects of treatment?

In order to have a better evaluation of our method and to achieve the best compliance of patients, this questionnaire was completed by each patient every year. To evaluate the comparison between the two groups, a statistics analysis regarding the achievement of expectations was conducted through the test.

Study

The clinical application of the above-mentioned products was conducted in the 170 patients of the study group who were affected by age-related skin diseases, intrinsic ageing and photo-damaged skin and was differentiated according to Table 1.

Table 1.

Expectations in patients with photo aging of the two groups and χ^2 value.

	Study group (n = 96)			*Control group (n = 34)*			χ^2
Expectations	**F**	**%**	**V_A**	**F**	**%**	**V_A**	
Extremely satisfied	44	45,8	8,7	0		1,7	
Satisfied	28	29,1	61,93	9	26,3	15,72	
Partially satisfied	19	19,8	10,47	20	59	12,32	26,21
Not satisfied	5	5,2	16,74	5	14,7	4,25	

F = Observed values
V_A = Awaited value

The patients, including the study group, were selected according to skin deseases:

1) Photo-ageing: 96 cases were enrolled after a macroscopic exam, in consideration of wrinkles, decreased skin tone (measured by pinch test), vascular collapse and signs of elastosis. The amount of collagen in the dermal skin of the fifty patients we tested using QMR technology have been previously evaluated with echograpy examination. The same ultrasound has been made to the patients of the control group. The patients' age varied from 28 to 65 years. The control group included 10 cases.
2) Actinic keratosis: 34 cases, from 47 to 78 years old.
   These cases where enrolled after clinical exam. Biopsies and histological examination where performed before and after the treatment (Figures 1, 2).
3) Intrinsic ageing: 40 cases, from 45 to 85 years old.

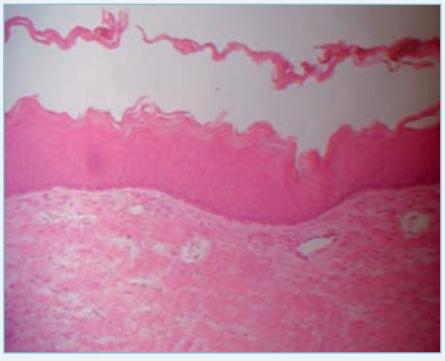


Figure 1.

Histology of actinic keratosis biopsy.

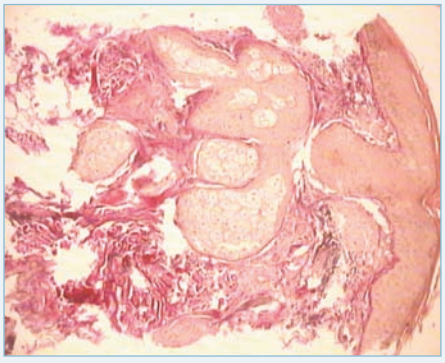


Figure 2.

Histology after 1 year of treatment.

These cases were enrolled in the study concerning Intrinsic ageing since all the patients involved, because of their life style, rigorously avoided sun exposure.

The control group includes:

1) Photo ageing: 34 cases, from 28 to 65 years old;
2) Actinic keratosis: 30 cases, from 47 to 78 years old;
3) Intrinsic ageing: 30 cases, from 67 to 85.

The same principles of the study group were applied to enroll the control group patients.

Results

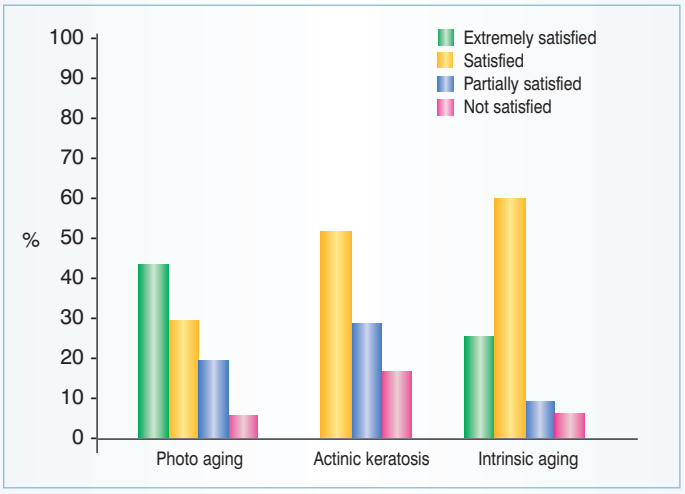
The clinical and statistical evaluation of the patients of the study group has shown (Graphic 1, Tables 1-4):

1) Patient with Intrinsic ageing (but patients simultaneously tested with QMR technology, who have been separated)
   - extremely satisfied: 24%
   - satisfied: 60%
   - partially satisfied: 10%
   - not satisfied: 6%
2) Patient with Actinic keratoses
   - extremely satisfied: none
   - satisfied: 53%
   - partially satisfied: 29,4%
   - not satisfied: 17,6%
3) Patient with Photo ageing (but patients simultaneously tested with QMR technology, who have been separated)
   - extremely satisfied: 43%
   - satisfied: 30%
   - partially satisfied: 20%
   - not satisfied: 7%
4) Expectations in patients with Photo ageing and Intrinsic ageing tested with the above-mentioned products plus QMR technology (Graphic 1.2)
   - extremely satisfied: 84%
   - satisfied: none
   - partially satisfied: 16%
   - not satisfied: none

The partially satisfied patients report in the commentary that their expectations are based on the combination between creams containing vitamin C and melatonin combined and collateral procedures such us botox, fillers, thermage (RF Ellman Advanged Thermage), laser or in

Graphic 1.

Perceptions of the improvement of the skin in the patients according to the skin problem after 3 years.



Graphic 1.2.

Perceptions of the improvement of the skin in patients who also underwent to QMR technology, according to the skin problem.

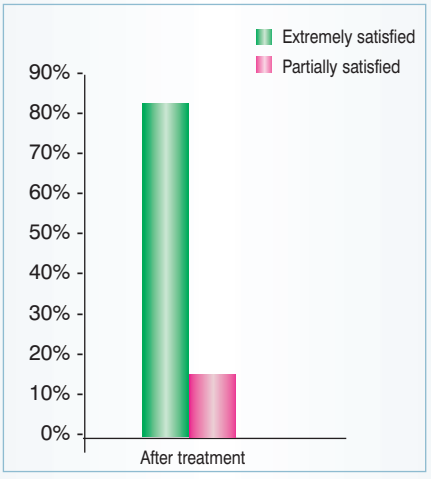


Table 2.

Expectations in patients with actinic keratosis among the two groups and χ^2 value.

	Study group (n = 34)			Control group (n = 30)			χ^2
Expectations	**F**	**%**	**V_A**	**F**	**%**	**V_A**	
Extremely satisfied							
Satisfied	18	53	10,68			8,43	
Partially satisfied	10	29,4	10,62	10	33,33	9,37	22,93
Not satisfied	6	17	13,81	20	66,4	12,18	

F = Observed values
V_A = Awaited value

Table 3.

Expectations in patients with intrinsic aging among the two groups and χ^2 value.

	Study group (n = 40)			Control group (n = 30)			χ^2
Expectations	**F**	**%**	**V_A**	**F**	**%**	**V_A**	
Extremely satisfied	10	25	1,33	0		1	
Satisfied	24	60	19,33	5	16,7	14,5	29,7
Partially satisfied	4	10	11,33	15	50	8,5	
Not satisfied	2	5	8	10	33,3	6	

F = Observed values
V_A = Awaited value

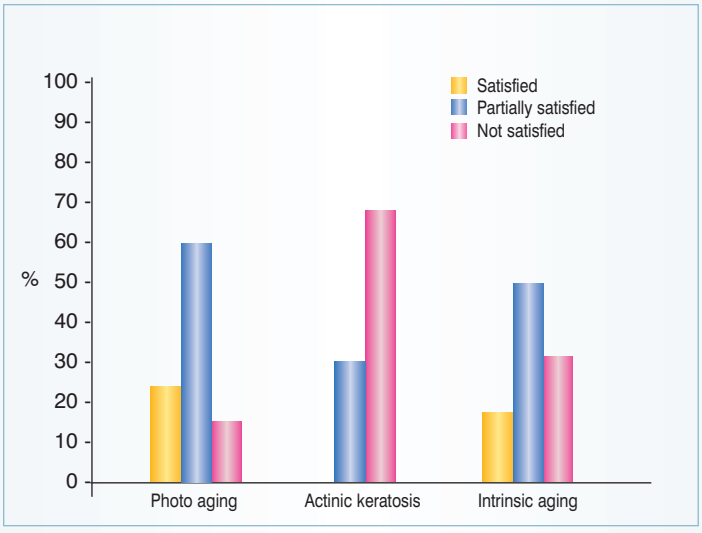
Table 4.

χ^2 value (until 10 degree of freedom).

G.L	p = 0.10	p = 0.05	p = 0.01	p = 0.005
1	2.705	3.841	6.635	7.879
2	4.605	5.991	9.210	10.597
3	6.251	7.815	11.345	12.838
4	7.779	9.488	11.277	14.860
5	9.236	11.07	15.086	16.749
6	10.645	12.592	16.812	18.547
7	12.017	14.067	18.475	20.278
8	13.362	15.507	20.090	21.955
9	14.684	16.919	21.666	23.589
10	15.987	18.307	23.209	25.188

Graphic 2.

Perceptions of the improvement of the skin in the control group according to the skin problem after 3 years.



certain cases surgery. The partially satisfied patients who underwent QMR report to be not fulfilled satisfied because their expectation was little bit higher than result could offer.

The clinical and statistical evaluation of the patients of the control group has shown (Graphic 2, Tables 1-4):

1) Expectations in patients with intrinsic ageing
   - 16,7% satisfied,
   - 50,0% partially satisfied,
   - 33,3% not satisfied yet.
2) Expectations in patients affected by actinic keratoses
   - 33,3% partially satisfied,
   - 66,4% not satisfied yet.
3) Expectations in patients with photo ageing
   - 26,3% satisfied,
   - 59,0% partially satisfied,
   - 14,7% not satisfied yet.

Statistical Analysis

We have employed the chi-squared test (χ^2) to demonstrate if the values of frequency we obtained are different in a significant way from the ones obtained through expected distribution; In this way we can demonstrate or refuse the hypothesis that the different treatments administered have the same effect or not.

From our study we obtained statistically significant differences, level of probability of 0.005.

Discussion

Both the study and control patients were given questionnaires asking them to express a judgment about their skin improvement during the three year period using their specific topical preparations. The questions were either yes or no or the scale of Likert (1 = "not at all satisfied" and 6 = "extremely satisfied").

Graph I demonstrates the compilation of the study group answers to the questionnaire.

What stands out is that of those affected by intrinsic aging, 24% thought they were extremely satisfied, 60% felt satisfied, 10% partially satisfied and 6% not satisfied with the treatment regimen.

All the patients treated with QMR technology plus products have been very satisfied and the sonography evaluation showed that two months after the end of the therapy the total amount of

collagen increased up to 15% (average), that means about 5-6% more than patients who did not underwent to synergic procedure using QMR technology.
In the study group of photoaging patients, 43% were extremely satisfied, 30% were satisfied, 20% partially satisfied and 7% not satisfied with the treatment regimen.
No one of the actinic keratosis patients felt extremely satisfied but 53% were satisfied, 29.4% partially satisfied and 17.6% were not satisfied. Of note, these patients almost all wan-

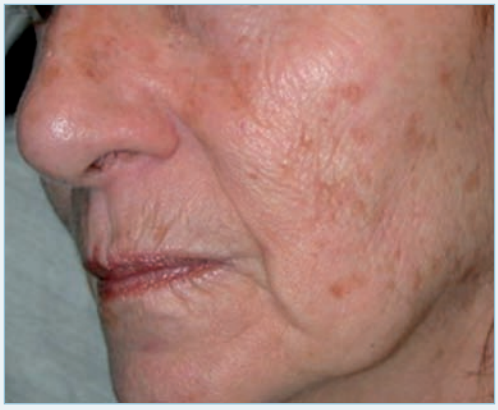


Figure 3.

Pre treatment.

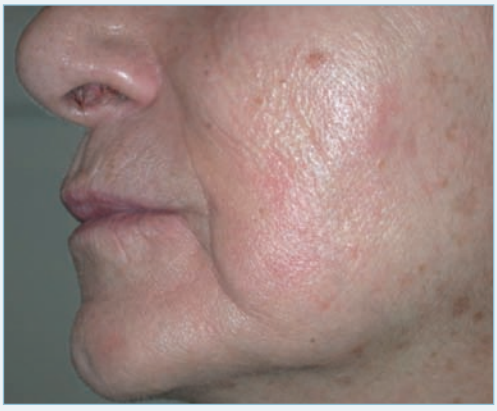


Figure 4.

Post treatment after 3 years.

Case 1.

A 64 year old patient heavy smoker, affected by skin aging, solar elastosis and in some areas actinic keratoses (Figure 1). The patient was 12 weeks under treatment with skin purify cleanser, purify toner, vitamin C fifteen serum with melatonin resveratrol and natural skin tone balancer with melatonin 1% and resveratrol cream in combination with restructurating melatonin 0.5% cream mixed with vitamins. Tretinoin 0.1% in a special formulation was added in the treatment once daily. The containing vitamin C and melatonin creams were applied twice daily for 12 weeks.
After that period the patient was introduced in a weekly maintenance program (Figures 3, 4).

Figure 5.

Pre treatment.

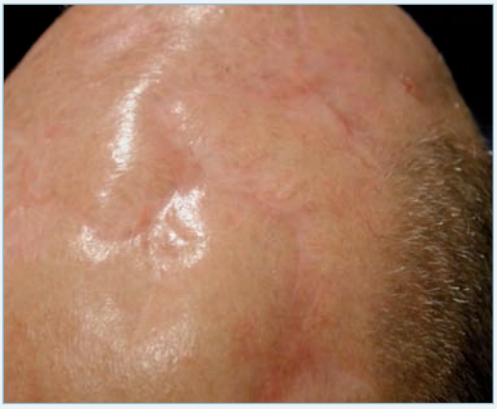


Figure 6.

Post treatment after 3 years.

Case 2.

The new protocol, was applied in cases with actinic keratosis, and we bring to example this 75 old patient affected by recurrent actinic keratosis and basal cell carcinoma. The patient was operated several times and the success rate was poor since the skin was undefended against the UV DNA damage. The patient was operated and the carcinoma was removed with local anesthesia thanks to the use of radiofrequency technology (Ellman Surgitron 4 Mhrz) and a new special silver alloy which does not create thermal damage. Multiple flaps were needed to cover the cranium under local anesthesia. The small areas where the bone was exposed were covered with equine collagen and fibrin glue. The creams were applied systematically daily starting from the post operative period. The protocol included cleanser, vitamin C serum, melatonin cream and special regenerating cream containing aloe. The products were applied 2 times a day. Exfoliating cream and tretinoin was added once a day after the healing process. The treatment was carried out for 6 months and a light peel was done after the first 8 weeks from the surgical period. The patient did not have any recurrence of precancerous lesions and is still following a maintenance program (Figures 5, 6).

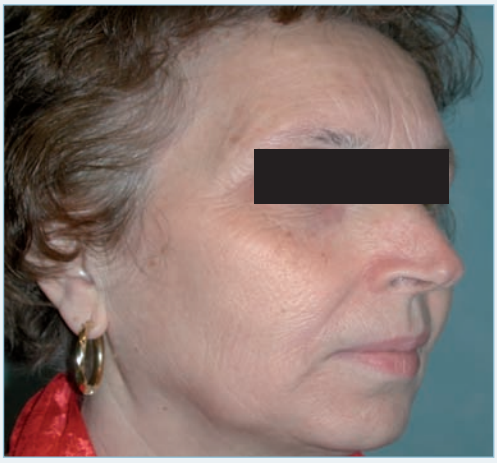


Figure 7.
Pre treatment.

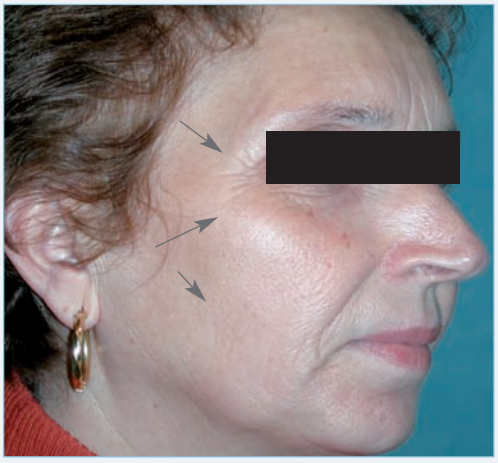


Figure 8.
Post treatment after 3 years.

Case 3.
This case represents a 70 years old patient affected by intrinsic aging. The patient has been treated for 3 years with our system which include vitamin C 15% serum containing melatonin and resveratrol, melatonin-resveratrol cream.
The before and after pictures show the effect of the treatment on skin due to the antioxidant properties of the system (Figures 7, 8).

Figure 9. *Pre treatment.*

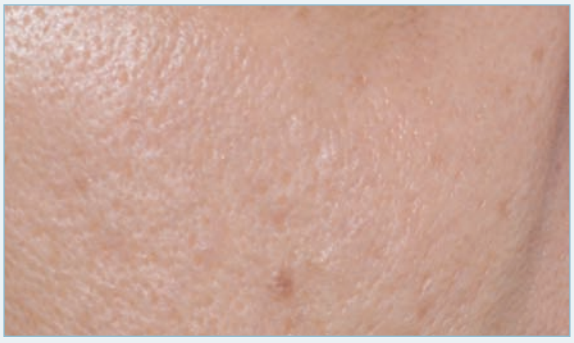
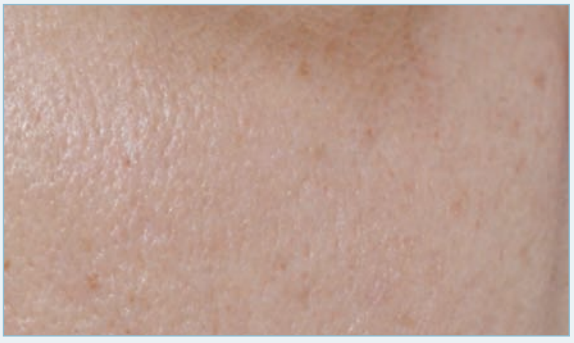


Figure 10. *Post treatment.*



Case 4.
This case represents a 56 years old patient affected by intrinsic aging. The patient has been treated with vitamin C 15% serum containing melatonin and resveratrol, melatonin-resveratrol cream twice a day plus QMR technology (8 procedures). Figures 9 and 10 show the right cheek of the same patient before and after the treatment. Skin texture is really improved.

ted additional surgical treatment (liquid nitrogen or curetting) in combination with the treatment regimen.
Graph II illustrates the compilation of the control group answers to the questionnaire. Not one patient in all categories of the control group was extremely satisfied. Only about 20% of the intrinsic aging and photoaging patients were satisfied. About 50% of these patients were only partially satisfied and about 30% were not satisfied.
The actinic keratoses patients showed that most were not satisfied with the control regimen and that about a third was partially satisfied. The difference between the study group and the control group has a statistical significance at a probability level of 0.5%.

Conclusion

As practicing clinicians most of us have seen the effects of using just moisturizers

to help improve the skin. This idea is illustrated in that the two groups both felt some satisfaction with the treatment protocols. However, more patients were significantly satisfied in the study group. The new melatonin multivitamin complex in combination with vitamin C 15% stabilized with melatonin, resveratrol and *Vitis vinifera*, improves the intrinsic aging and photo-aged skin.

In addition, combining this with tretinoin may be considered as an alternative treatment for the prevention of actinic keratoses and photo damaged skin. QMR technology improves significantly the results increasing the amount of collagen and ameliorating the skin texture. This new protocol may be used to treat photo-damaged skin diseases and as an anti-aging cosmetic treatment. The three case studies point out how versatile the new products are for treating a variety of skin ailments. More studies need to be done to objectively show the effects these medications have on the skin.

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