Q'URNAILTM in Treatment of Onichomycoses.

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Q'URNAILTM - გამოყენება ორნიქომიკოზის დროს

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TECHNOLOGICAL APPROACH

Q'urNail™ represents one of the targeted product from QurSkin Family™ group produced by QurTech, Inc. QurSkin Family™ products are the comprehensive formulas that help to fight bacteria and other microscopic invaders (germs).

Scientific research and nanotechnological advancements made it possible to combine proven Anti-Bacterial Substances, Antioxidants and Self-healing NANO-COMPLEXES™ into a singular personal care formula increasing efficiency of functional ingredients. QurSkin Family™ represents absolutely new nanotechnological approach in Skin Barrier System.

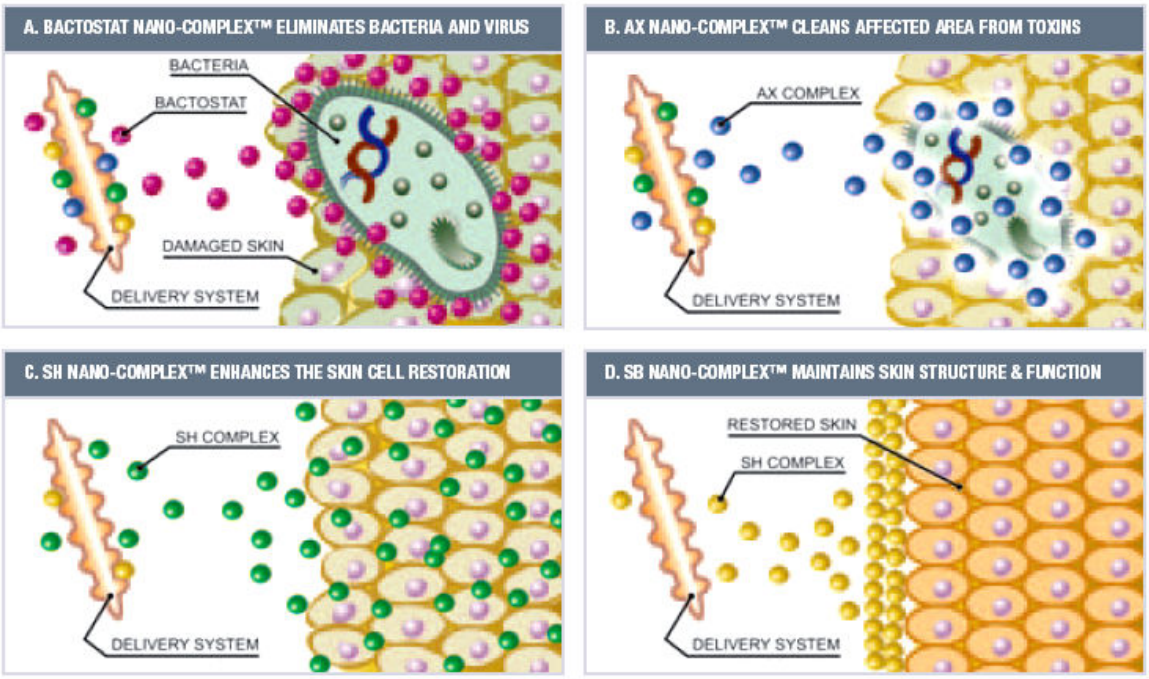
NATURE OF THE PROBLEM

Onichomycosis, a fungal infection of the nail bed and nail plate, account for approximately 50% of all nail diseases [1, 6, 11] and are the most common disorder in adults, affecting up to 18.5% of US adult population[1, 2, 9]. Antibiotics, illnesses, injuries and cortisone preparations increase person's risk of fungal infections. In this regard Onichomycoses are considered as a tangible mycological problem and exploration of new ways of treatment is important.

This article describes effectiveness of new technological approach in topical treatment of Onichomycoses.

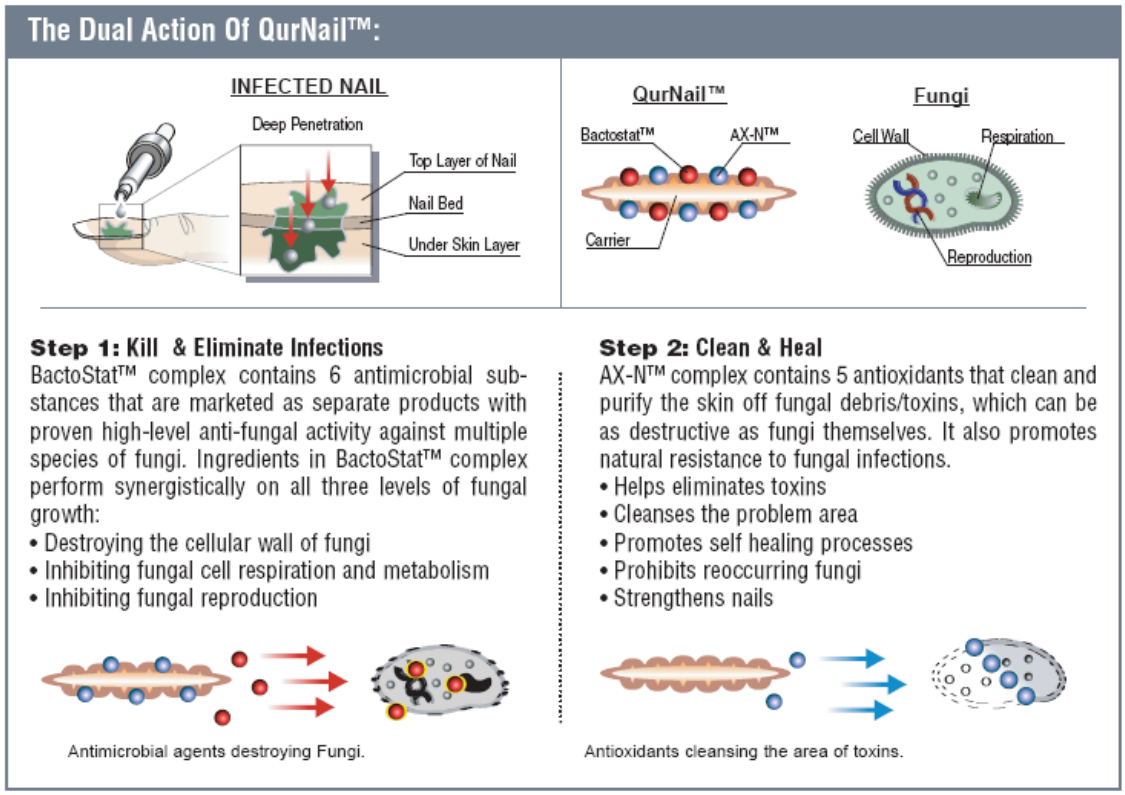
HOW QURSKIN FAMILY™ PRODUCTS WORK?

Based on scientific advancements in nanotechnology, QurSkin Family™ products combine multiple proprietary bioactive NANO-COMPLEXES™ into a singular formula. Substances composed QurSkin Family™ has been individually proven as powerful antimicrobial agents. They are marketed as separate products with high-level anti-microbial activity against multiple species of gram-positive and gram-negative bacteria and their spores. Bellow is the diagram explaining the mechanism of action of QurSkin Family™ products.



Dual Action: Q'urNail™ represents a new generation of combined personal care products designed to treat Onychomycoses and Skin Fungal Infections. Q'urNail™ combines two proprietary bioactive complexes – BactoStat™ and AX-N™ – into a singular personal care formula. Simultaneous action of the ingredients in Q'urNail™ remarkably increases the natural self-healing processes, helping eliminate bacteria and fungus.

All NANO-COMPLEXES™ are incorporated into a proprietary developed Liquid Matrix Delivery System, providing stabilization of active substances and their targeted delivery with deep penetration to affected tissues.



When Q'urNail™ is applied to the skin and nail, the formulation creates what is called phase separation - separates the layers of matrix delivery system to create tiny slippery spaces – micro-pathways. This allows molecules of active substances to slide through. Via these micro-pathways, the active ingredients are delivered therapeutically to the affected tissues of nail and the skin. This prevents additional damage of the skin and also protects from generation of pro-inflammatory insults which contribute to chronic inflammation. A diagramed projection of Q'urNail™ is shown bellow:

--FST---NAX---FST---NAX---FST---NAX---FST---NAX---FST--
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Note: **FST** - anti-fungal and anti-bacterial nanocomplex (BactoStat™)
NAX - natural anti-oxidants nanocomplex (AX-N™)
- - - - matrix delivery system

MATERIAL

We analyzed data of 113 patients with Onichmycoses treated during the period of 2005-2007 in 10 podiatric offices in New York area.

Table 1: Division of Patients by Gender and Age

Gender	Age					Total
	30-39	40-49	50-59	60-69	70 and up	
Male	5	30	21	7	0	63
Female	2	26	16	4	2	50
Total	7	56	37	11	2	113

In all 113 patients fungal infection was located at toenail area. Singular nail affection was registered in 99 and multiple nails were affected in 14 patients.

In 51 patients clinical diagnosis of Onichmycosis was supported with mycological study of affected nail and skin tissue. Among them in 23 patients mycological studies were repeatedly performed after treatment. In 62 patients the diagnosis was based only on clinical observations.

In 86 patients Q'urNail™ was used as an only topical treatment. 8-10 drops of Q'urNail™ were applied over the affected toenail twice a day (Group #1). In 27 patients' topical treatment with Q'urNail™ was combined with systemic treatment with Lamisil (Terbinafine) 250 mg. one tablet every other day for 3 months (Group #2).

Table 2: Division of Patients According to Clinical Features of Onichomycosis

Clinical Feature	Group 1	Group 2	Total
Toenails Affected:			
one	80	19	99
more than one	6	8	14
Depth of Tissue Affection:			
nail matrix only	68	6	74
nail matrix + nail bed	18	21	39
Onichomycosis Subtype:			
Distal Subungual Onichomycosis (DSO)	76	16	92
Superficial White Onichomycosis (SWO)	9	6	15
Proximal Subungual Onichomycosis (PSO)	1	5	6
Clinical Signs:			
nail discoloration	86	27	113
roughened and crumbled nail	86	27	113
a thickened and opacified nail plate	73	25	98
swelling of the nail fold	8	16	24
involvement of surrounding skin	1	5	6

To optimize the goal of study a Q'urNail™ 'Clinical Study Chart' was prepared and added to patient's regular chart. Dynamic observations of clinical signs were performed by qualified podiatrist every two weeks. Each clinical sign was graded from 5 to 0 depending to visual estimation of changes. Average treatment period we could observe from patients' charts was 16 weeks.

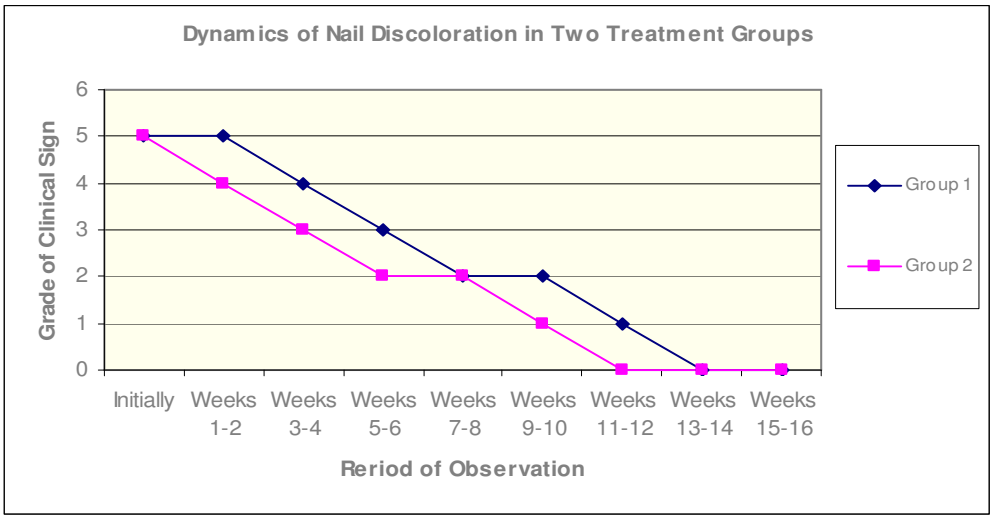
RESULTS AND DISCUSSION

The results of 16-week clinical observations are shown in series of the following tables and diagrams

Table 3: Dynamics of Changes in Nail Discoloration

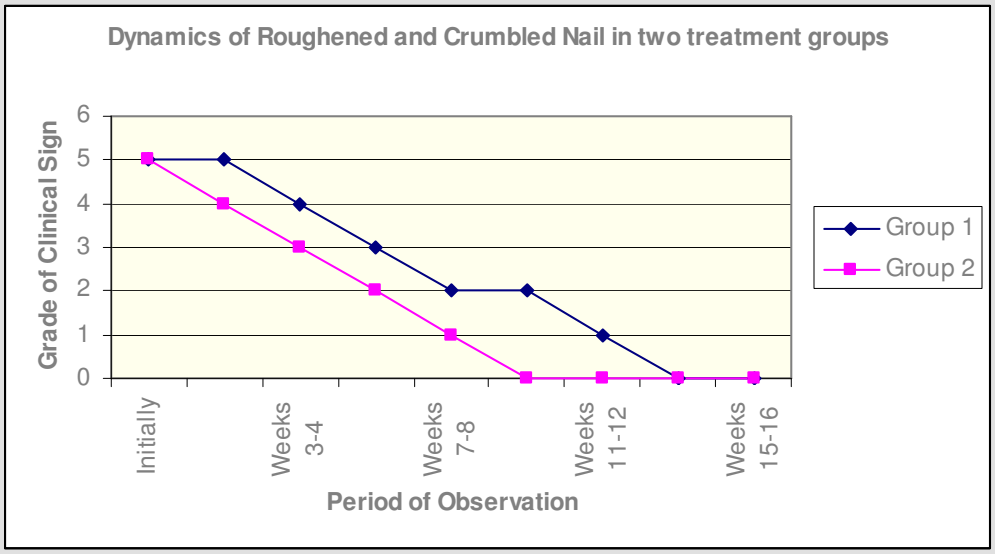
Group	Grade of Nail Discoloration								
	Initially	Weeks 1-2	Weeks 3-4	Weeks 5-6	Weeks 7-8	Weeks 9-10	Weeks 11-12	Weeks 13-14	Weeks 15-16
Group 1	5	5	4	3	2	2	1	0	0
Group 2	5	4	3	2	2	1	0	0	0

Diagram 1: Dynamics of changes in Nail Discoloration



As shown in Table 3 and Diagram 1, the average time of restoration of nail discoloration in two groups of patients was from 11 to 14 weeks. The grayish-yellow and grayish-white spots in distal parts of nail and lateral nail fold area gradually faded to normal nail color. In both groups this process was going in parallel, but in Group 2 restoration of nail discoloration was resorbed about two weeks faster than in Group 1, which means that the combination of Lamisil with Q'urNailTM gives earlier results in restoration of nail color.

Table 4: Dynamics of Changes in Roughened and Crumbled Nail



Group	Grade of Roughened and Crumbled Nail								
	Initially	**Weeks 1-2**	**Weeks 3-4**	**Weeks 5-6**	**Weeks 7-8**	**Weeks 9-10**	**Weeks 11-12**	**Weeks 13-14**	**Weeks 15-16**
Group1	5	5	4	3	2	2	1	0	0
Group2	5	4	3	2	1	0	0	0	0

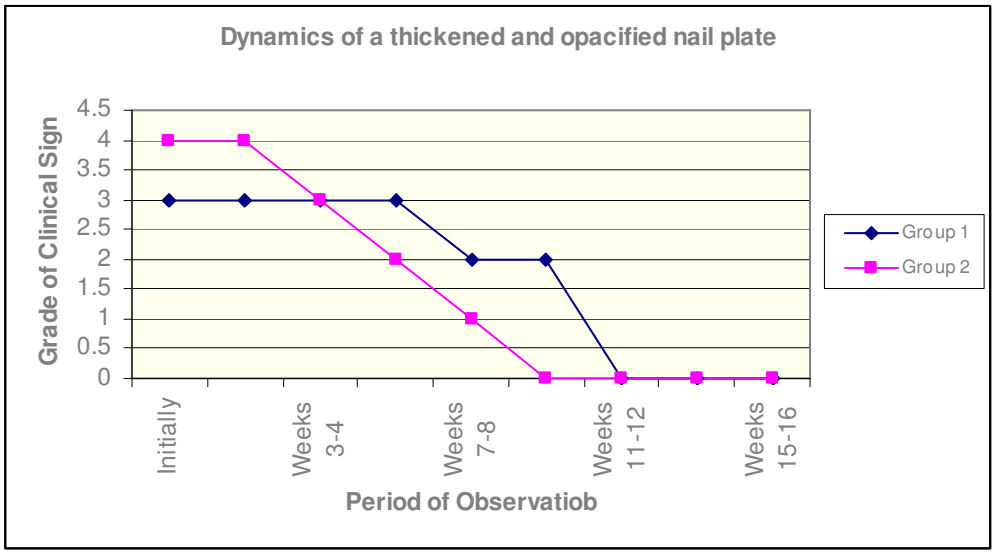
Diagram 2: Dynamics of Changes in Roughened and Crumbled Nail

Improvement of roughened and crumbled nail (Table 4 and Diagram 2) was going in parallel in both groups up to 8th week of observation. Then in Group 1 the process of improvement showed signs of slow down at the beginning of week 8 and continued up to week 10. After that improvement was continued up to visually complete stop of nail disfiguration at week 13. In Group 2 the process of improvement went proportionally and at week 9 the process of nail disfiguration was visually stopped.

Table 5: Dynamics of Changes in a Thickened and Opacified Nail Plate

Group	Grade of a Thickened and Opacified Nail Plate								
	Initially	Weeks 1-2	Weeks 3-4	Weeks 5-6	Weeks 7-8	Weeks 9-10	Weeks 11-12	Weeks 13-14	Weeks 15-16
Group 1	3	3	3	3	2	2	0	0	0
Group 2	4	4	3	2	1	0	0	0	0

Diagram 3: Dynamics of changes in a Thickened and Opacified Nail Plate



Signs of thickened and opacified nail plate (Table 5 and Diagram 3) in Group 1 did not showed any improvement up to end of week 6 after which improvement went rapidly and at the beginning of week 11 the progress of nail thickening and opacification was visually stopped. In Group 2 improvement of thickening and opacification of nail plate showed relatively proportional progress and was visually complete at week 10.

Table 6: Dynamics of changes in Swelling of Nail Fold

Group	Grade of Swelling of Nail Fold								
	Initially	Weeks 1-2	Weeks 3-4	Weeks 5-6	Weeks 7-8	Weeks 9-10	Weeks 11-12	Weeks 13-14	Weeks 15-16
Group 1	3	3	3	2	2	1	0	0	0
Group 2	3	3	2	2	1	0	0	0	0

Diagram 4: Dynamics of changes in Swelling of Nail Fold

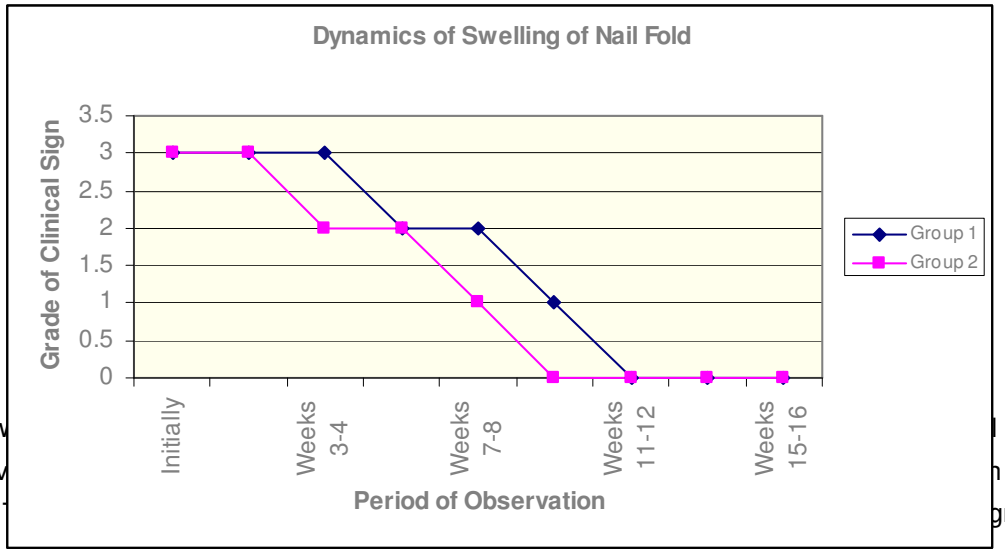


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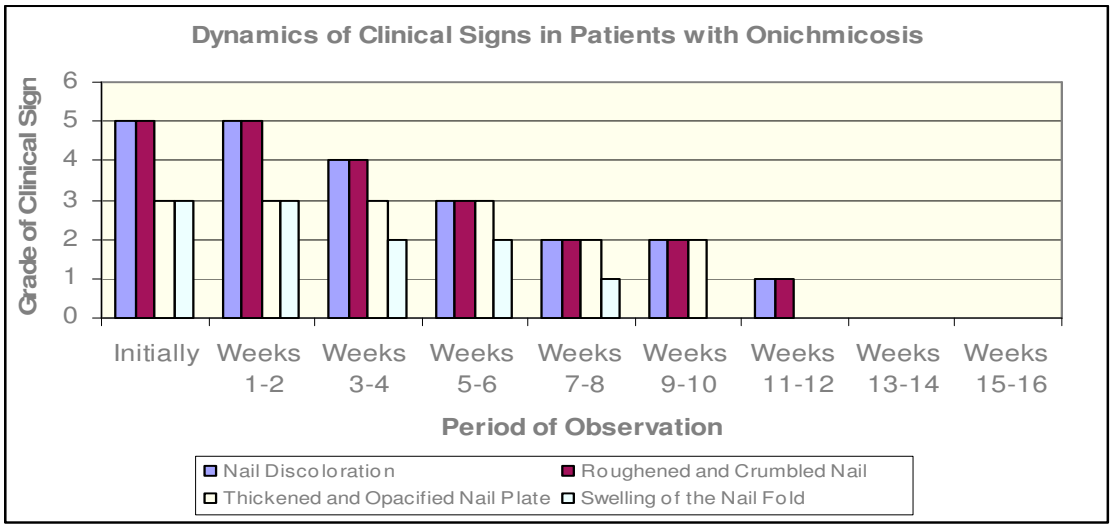
Table 7: Dynamics of Clinical Signs Improvement

Clinical Sign	Initially	Weeks 1-2	Weeks 3-4	Weeks 5-6	Weeks 7-8	Weeks 9-10	Weeks 11-12	Weeks 13-14	Weeks 15-16
Nail Discoloration	5	5	4	3	2	2	1	0	0
Roughened and Crumbled Nail	5	5	4	3	2	2	1	0	0
Thickened and Opacified Nail Plate	3	3	3	3	2	2	0	0	0
Swelling of the Nail Fold	3	3	2	2	1	0	0	0	0

Diagram 5: Dynamics of clinical signs improvement during 16-week period of observation

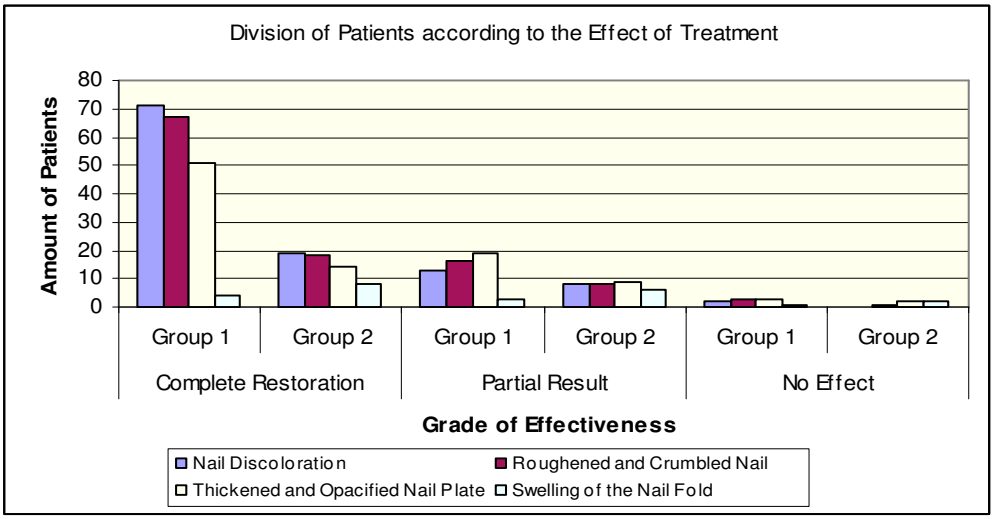


According to results of treatment all patient were divided into three groups: "Complete Restoration" when clinical signs of Onichomycosis were visually eliminated completely, "Partial Results" when condition of affected nails was improved, but some signs of nail affection were remain and "No Effect" when the treatment efforts were graded as ineffective. Table 8 and Diagram 6 show this division.

Table 8: Division of Patients According to the Results of Treatment

Clinical Sign	Complete Restoration				Partial Result				No Effect			
	Group 1		Group 2		Group 1		Group 2		Group 1		Group 2	
Nail Discoloration	71	82.5%	19	70.4%	13	15.1%	8	29.6%	2	2.4%	0	0
Roughened and Crumbled Nail	67	77.9%	18	66.7%	16	18.6%	8	29.6%	3	3.5%	1	3.7%
Thickened and Opacified Nail Plate	51	69.8%	14	56.0%	19	26.0%	9	36.0%	3	4.2%	2	8.0%
Swelling of the Nail Fold	4	50.0%	8	50.0%	3	37.5%	6	37.5%	1	12.5%	2	12.5%

Diagram 6: Division of Patients According to the Results of Treatment



As shown in Table 8 complete restoration of nail discoloration was registered in 82.5% in Group 1 and in 70.4% in Group 2. During the treatment period areas of discoloration gradually faded and disappeared. In case of 'Partial Results' "very light spots" of discoloration were still remaining at the end of 16th week of treatment. Patients were advised to continue apply Q'urNail™ additional 2-3 week until complete resolution of nail discoloration. 'No Effect' was observed in 2.4% (2 patients) of Proximal Subungual Onichomycosis (PSO). In both of these cases nail plate was highly hypertrophic and deformed what probably broke down penetration of active substances to the affected tissues.

Roughened and Crumbled Nail was completely restored in 77.9% in Group 1 and in 66.7% in Group 2. Partial Results were observed in 18.6% in Group 1 and in 29.6% in Group 2.and all 'No Effect' results (3.5% - Group 1 and 3.7% - Group 2) were observed in patients with Proximal Subungual Onichomycosis (PSO).

Thickened and Opacified Nail Plate was completely restored in 69.8% in Group 1 and in 56.0% in Group 2. Partial results were achieved in 26% in Group 1 and in 36% in Group 2. In 4.2% (Group 1) and 8.0% (Group 2) treatment of Thickened and Opacified Nail Plate sign was ineffective.

Swelling of the Nail Fold was completely treated in 50.0%, partially treated in 37.5% and ineffective in 12.5% in both groups of patients.

'Complete Restoration' was registered in average in 70.0% in Group 1 and in 60.8% in Group 2. It should be noted that in all cases 'Complete Restoration' of signs of Onichomycosis in Group 2 was observed 14-18 days earlier than in Group 1. Most probably this effect is due to combined use of systemic treatment with Lamisil and topical application of Q'urNail™.

According to published data [3, 4, 8] the effectiveness of the solo use of Lamisil in treatment of Onichomycosis fluctuates in 62-68% with every day intake of 250 mg. during 4-6 months. High probability of hepatotoxic side effects of this medication is indicated. In our observations in Group 2 the cumulative dosage of Lamisil was reduced twice, because patients were taking 250 mg. of medication every other day in combination with daily applications of Q'urNail™. Hepatotoxic effects of Lamisil were not registered and 'Complete Restoration' was achieved in 60.8%. Duration of treatment was shortened to 9-11 weeks. All these point that Q'urNail™ can become an effective part in cases requiring combined systemic and topical treatment.

Despite of the opinion that topical treatments alone are generally unable to cure Onichomycosis because of insufficient nail plate penetration [8, 12], our findings showed that 'Complete Restoration' in Group 1 was achieved in 70.0%. We think such a "high" rate of 'Complete Restoration' was acheived due to facilitated delivery of antifungal complex by liquid matrix delivery system providing targeted delivery and deep penetration to affected tissues. At the same time positive changes developed slowly – about 2-3 weeks later than in Group 2.

Published data indicate that for toenail Onichomycosis, mycologic cure rates (ie, obtaining negative laboratory results) with standard terbinafine therapy are 35-50%. [12] Success rates with Q'urNail™ treatment alone was comparable with that data – 45.8%.

Subjectively, patients reported satisfaction with Q'urNail™ alone treatment compared with combined treatment with Lamisil + Q'urNail™.

'Partial Results' were registered in average in 24.3% in Group 1 and in 33.2% in Group 2. 'No Effect' was observed in 5.6% in Group 1 and in 8.0% in Group 2. Some researchers indicate that after standard dosing of treatment and achievement of cure, nails may continue to look dystrophic [5, 7, 10]. If we accept that point of view, than the achievement of 'Partial Results' can be considered as satisfactory. It also should be noted, that all cases of 'Partial Results' were observed in deep affection of tissues: nail matrix + nail bed. We can not exclude that continuation of treatment (at least topical) for several more weeks could bring patients to 'Complete Restoration'. But this is a subject of our further observations.

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რეზიუმე:

მოტანილია პრეპარატ Q'URNAIL™ გამოყენების შედეგები ორნიქომიკოზით დაავადებულ 113 პაციენტში,რომლებიც მკურნალობდნენ 2005-2007წწ. ნიუიორკის პედიატრიულ კლინიკებში. მათგან 99 ჰქონდა დაავადების მარტივი, ხოლო 14 – რთული ფორმა.
პრეპარატი მომზადებულია ნანოტექნოლოგიურ პრინციპებზე. მას აღმოაჩნდა ანტიბაქტერიული და ანტიფუნგური ეფექტი. ის სპობდა როგორც გრამ დადებით,ასევე გრამუარყოფით ბაქტერიებს და მათ სპორებს.
ამასთან პრეპარატს ჰქონდა ანტიოქსიდანტური ეფექტი. მოყვანილია პრეპარატის დანიშვნის ჩვენებები, დოზები და მკურნალობის ხანგრძლივობა.

References:

1. Andre J, Achten G. Onychomycosis. Int J Dermatol. Oct 1987;26(8):481-90.

2. Baran R, Hay RJ, Tosti A, Haneke E. A new classification of onychomycosis. Br J Dermatol. Oct 1998;139(4):567-71.

3. Crawford F, Young P, Godfrey C, et al. Oral treatments for toenail onychomycosis: a systematic review. Arch Dermatol. Jun 2002;138(6):811-6.

4. Cribier BJ, Paul C. Long-term efficacy of antifungals in toenail onychomycosis: a critical review. Br J Dermatol. Sep 2001;145(3):446-52.

5. Evans EG. Causative pathogens in onychomycosis and the possibility of treatment resistance: a review. J Am Acad Dermatol. May 1998;38(5 Pt 3):S32-56.

6. Faergemann J, Baran R. Epidemiology, clinical presentation and diagnosis of onychomycosis. Br J Dermatol. Sep 2003;149 Suppl 65:1-4.

7. Gupta AK, Scher RK, De Doncker P. Current management of onychomycosis. An overview. Dermatol Clin. Jan 1997;15(1):121-35.

8. Hull PR. Onychomycosis--treatment, relapse and re-infection. Dermatology. 1997;194 Suppl 1:7-9.

9. Kemna ME, Elewski BE. A U.S. epidemiologic survey of superficial fungal diseases. J Am Acad Dermatol. Oct 1996;35(4):539-42.

10. Odom RB. New therapies for onychomycosis. J Am Acad Dermatol. Sep 1996;35(3 Pt 2):S26-30.

11. Scher RK. Onychomycosis: a significant medical disorder. J Am Acad Dermatol. Sep 1996;35 (3 Pt 2):S2-5.

12. Sigurgeirsson B, Olafsson JH, Steinsson JB, et al. Long-term effectiveness of treatment with terbinafine vs itraconazole in onychomycosis: a 5-year blinded prospective follow-up study. Arch Dermatol. Mar 2002;138(3):353-7.