

# APPLICATION OF COSMETIC NAIL VARNISH DOES NOT AFFECT THE ANTIFUNGAL EFFICACY OF AMOROLFINE 5% NAIL LACQUER IN THE TREATMENT OF TOENAIL ONYCHOMYCOSIS: RESULTS OF A RANDOMIZED ACTIVE-CONTROLLED STUDY AND *IN VITRO* ASSAYS

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## STATEMENT OF PURPOSE

- The objective of this set of studies, combining clinical *in vivo* and experimental *in vitro* investigations, was to evaluate whether the antifungal efficacy of amorolfine 5% nail lacquer (NL) is affected by masking cosmetic nail varnish applied 24 hours or 10 minutes later.

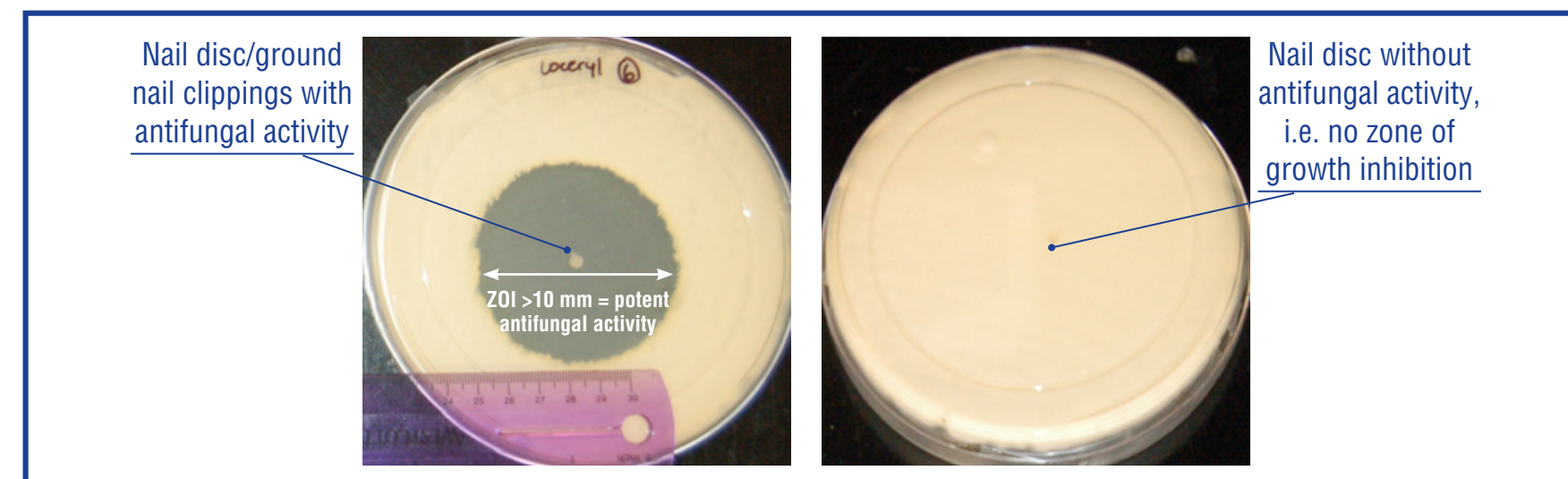
## LITERATURE REVIEW

- Onychomycosis is a common, unsightly disease<sup>1,2</sup>.
- Patients reportedly apply cosmetic nail varnish on top of amorolfine 5% NL (Loceryl®, Galderma SA, Lausanne, Switzerland) to mask their toenail disease despite the lack of previous studies on possible interactions between amorolfine 5% NL and cosmetic nail varnish.

## METHODOLOGY

### CLINICAL STUDY DESIGN

- Single site, investigator-blinded, parallel-group comparison study.
- Subjects randomized 1:1 to receive 12 weeks treatment of:
  - amorolfine 5% NL alone
  - amorolfine 5% NL plus Forever Strong Super Stay 7 days nail varnish (ivory rose color; Maybelline) applied 24 hours later.
- Subjects with at least one big toenail affected by mild to moderate distal subungual onychomycosis (DSO).
- Clippings of affected toenails collected at week 12 were ground down and 2 mg transferred to the center of an agar plate seeded with *Trichophyton mentagrophytes*.
- Measurement of zone of inhibition (ZOI) of fungal growth were measured after 5 days incubation at 35°C:



- Subungual debris collected at week 12 was analyzed to detect and identify any living fungus present.

## IN VITRO ASSAYS

- Human cadaver non-diseased big toenails:
  - group 1 untreated nail
  - group 2 amorolfine 5% NL alone (25 µL/cm<sup>2</sup>)
  - group 3 amorolfine 5% NL + one of 11 different brands of nitrocellulose-based cosmetic nail varnish applied 10 minutes later
  - group 4 amorolfine 5% NL + one of 11 different brands of nitrocellulose-based cosmetic nail varnish applied 24 hours later.
- Disks (N=6 per test condition) of nail were placed (treated side upwards) at the center of agar plates seeded with *T. rubrum*.
- ZOI were measured after 4 days at 30°C.

## RESULTS

### SUBJECTS

- Of 98 subjects screened, 50 subjects with both positive direct microscopy and culture results were enrolled (Table 1).

**Table 1.** Demographic and baseline characteristics (intent-to-treat)

	Amorolfine 5% NL (N=24)	Amorolfine 5% NL + Cosmetic varnish (N=26)	Total (N=50)
Male gender, n (%)	20 (83.3)	19 (73.1)	39 (78.0)
Age, years			
Mean ± SD	53.7 ± 12.5	55.1 ± 12.0	54.4 ± 12.1
White race, n (%)	24 (100.0)	26 (100.0)	50 (100.0)
Phototype, n (%)			
I	1 (4.2)	0 (0)	1 (2.0%)
II	5 (20.8)	4 (15.4)	9 (18.0%)
III	18 (75.0)	22 (84.6)	40 (80.0%)
Onychomycosis duration			
< 1 year	2 (8.3%)	2 (7.7%)	4 (8.0%)
1 to 5 years	10 (41.7%)	5 (19.2%)	15 (30.0%)
> 5 years	12 (50.0%)	19 (73.1%)	31 (62.0%)
Positive mycological examination (direct microscopy and culture)	24 (100.0%)	26 (100.0%)	50 (100.0%)
Number of affected nails			
Mean ± SD	5.7 ± 2.4	5.9 ± 3.3	5.8 ± 2.9

## EFFICACY

- Mycological cultures of subungual debris from treated diseased nails at week 12 were negative for dermatophytes and non-dermatophyte nail pathogens for all subjects in both groups (Table 2).

**Table 2.** Mycological analyses at week 12 (intent-to-treat)

	Amorolfine 5% NL (N=23)	Amorolfine 5% NL + Cosmetic varnish (N=25)	P value
Diameter of ZOI (mm)			
Mean ± SD	53.5 ± 6.2	53.6 ± 9.1	0.942
Median (min-max)	54.0 (41-63)	54.0 (27-70)	
Negative culture	23 (100.0%)	25 (100.0%)	

- Mean diameters of zones of inhibition for affected nail clippings from subjects in both groups were similar (Table 2 and Fig. 1).
- Most subjects (88%) in the nail varnish group indicated that the cosmetic varnish masked their toenail disease and representative photographs are shown in Fig. 2.

## SAFETY

- One subject in the amorolfine 5% NL plus cosmetic nail varnish group had a non-treatment-related dermatologic adverse event (hematoma under the nail).

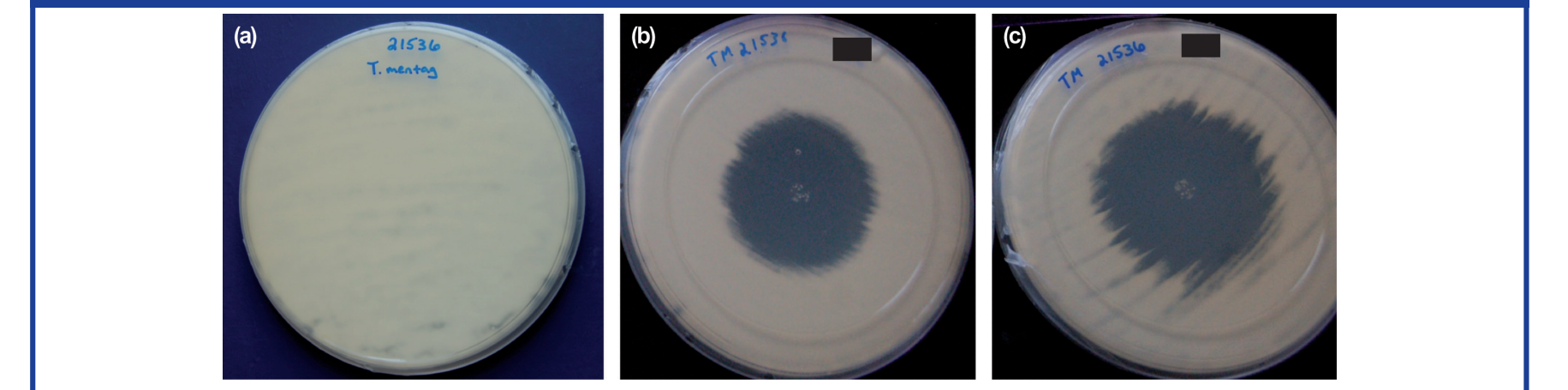
## IN VITRO ASSAYS

- The mean ZOI for amorolfine 5% NL plus the cosmetic nail varnish used in the clinical study (Forever Strong Super Stay) (shown in dark blue) was similar to the active control of amorolfine 5% NL alone (shown in red) (Fig. 3).
- Nails coated with one of 11 cosmetic nail varnishes, applied 10 min (Fig. 3a) or 24 hours (Fig. 3b) after amorolfine 5% NL application, all gave zones of inhibition (> 40 mm) representing potent antifungal activity.

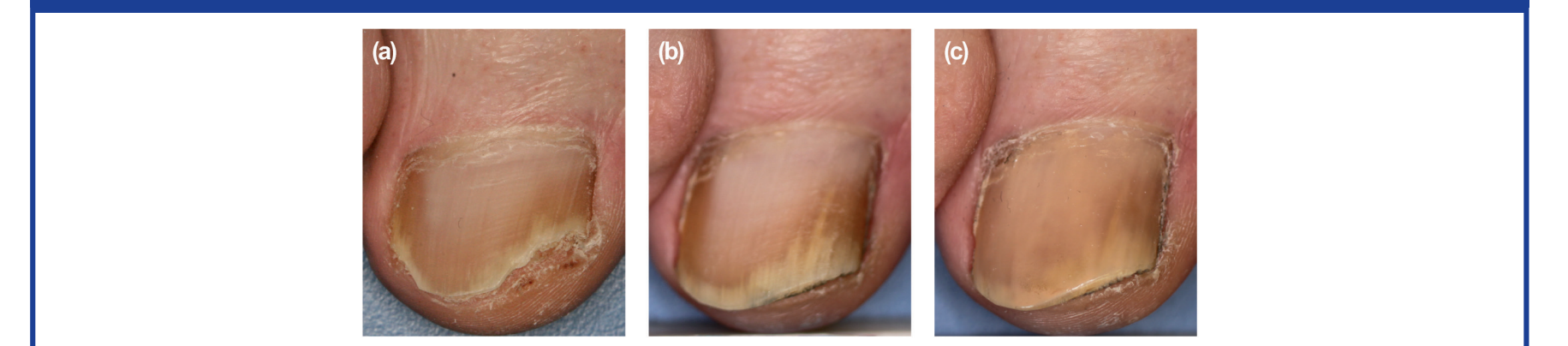
## DISCUSSION

- As previous publications had reported a higher incidence of onychomycosis in men<sup>1,2</sup>, a pale, natural-colored cosmetic nail varnish was chosen for this study so that it could appeal to both men and women to conceal their diseased nails.
- All the best-selling nitrocellulose-based nail varnishes used in the *in vitro* assays had no effect on the antifungal efficacy of amorolfine 5% NL; they included darker colored nail varnishes with even better coverage to mask diseased nails.
- In conclusion, based on these results, cosmetic nail varnish applied post-amorolfine had no effect on the subungual antifungal activity of amorolfine 5% NL or its penetration through toenails.

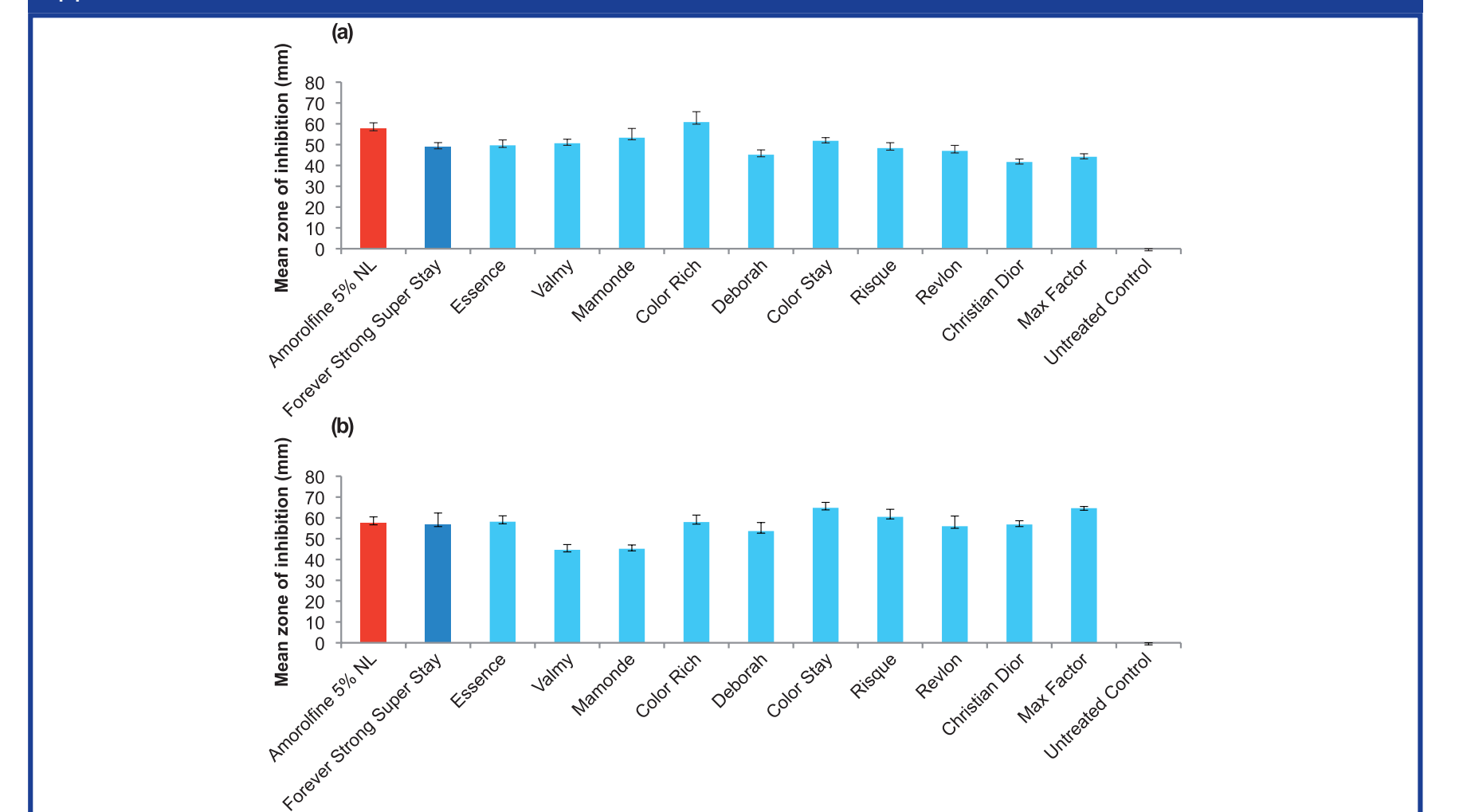
**Figure 1.** Representative seed plates of *Trichophyton mentagrophytes* showing an untreated nail control (a), a zone of inhibition from ground nail clippings collected after 12 weeks of treatment from a subject in the amorolfine 5% NL alone group (b), and from a subject in the amorolfine 5% NL plus cosmetic nail varnish group (c).



**Figure 2.** Representative photographs of an affected toenail at baseline (a) and after 12 weeks treatment with amorolfine 5% NL plus cosmetic nail varnish showing the appearance without the masking effect of the cosmetic nail varnish (b), and with cosmetic nail varnish (c).



**Figure 3.** Mean diameters of ZOI in *in vitro* assays of human toenails which received amorolfine 5% NL alone compared to toenails which received cosmetic nail varnishes 10 minutes (a) or 24 hours (b) after application of amorolfine 5% NL.



## REFERENCES

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