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          360          370          380          390          400          410
800039  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800041  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900044  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900046  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800024  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800025  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800044  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800036  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800037  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900038  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800035  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800038  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800043  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900039  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900047  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900043  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800030  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900040  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800022  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800023  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800040  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
900041  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
800026  RNLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQSLYSIFAAGDPNLKVLQRGCFRYFQ
Ay12   RDLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQAALYSIFAAGDPNLKVLQRGCFRYFQ
AY11   RDLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQALYSIFAAGDPNLKVLQRGCFRYFQ
DQ     RDLLSPEAVPDLSDTKLVLKQLSKFHWQRKSLISVINILAQALYSIFAAGDPNLKVLQRGCFRYFQ
Clustal Consensus *:*****:***:*****

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AY12 = AY282412; AY11= AY282411; DQ = DQ060522

Fig S1: Multiple sequence alignment of squalene epoxidase of terbinafine resistant strains of *Trichophyton rubrum* demonstrating F397L non-synonymous mutation in some of the resistant strains. Only partial sequence is shown here.

Table S1: Reports on terbinafine susceptibility of *T. rubrum* and *T. interdigitale*

S L no	Year	Author (reference no.)	Country	Patient sample	Growth of dermatophyte	Species (No.)			Terbinafine MIC in mg/L			Onychomycosis cases only	Nail, hair and skin involvement
						Organism	MIC <sub>50</sub>	MIC <sub>90</sub>	GM				
1	2017	Yamada <i>et al.</i> (1)	Japan	2056	2056	<i>T. rubrum</i> (1644)	0.1-	12.8 <sup>#</sup>	-	-	-	Yes	
						<i>T. interdigitale</i> (412)	3.2*	-					
2	2016	Baghi <i>et al.</i> , (2)	Iran	100	100	<i>T. rubrum</i> (29)	0.063	0.25	0.06	-	-	Yes	
						<i>T. interdigitale</i> (52)	0.063	0.25	0.007 1				
3	2016	Mohd Nizam <i>et al.</i> (3)	Malaysia	11	11	<i>T. rubrum</i> (3)	-	2-4 <sup>#</sup>	3.17	-	-	Yes	
						<i>Trichophyton</i> spp (7)	-	0.06- 0.12 <sup>#</sup>	0.08				
4	2011	Ansar <i>et al.</i> (4)	Iran	316	316	<i>T. interdigitale</i> (156)	0.016	0.125	0.017	-	-	Yes	
						<i>T. rubrum</i> (60)	0.016	0.063	0.017				
5	2013	Adimi <i>et al.</i> (5)	Iran	320	320	<i>T. rubrum</i> (89)	0.031 2	16	0.172	-	-	Yes	
						<i>T. mentagrophytes</i> (136)	0.031 2	16	0.142				
6	2014	Silva <i>et al.</i> (6)	Brazil	216	70	<i>T. interdigitale</i> (24)	<0.03 1	<0.031	0.03	-	-	Yes	
						<i>T. rubrum</i> (37)	<0.03 1	<0.031	0.06				

7	2010	Magagnin <i>et al.</i> (7)	Brazil	26	26	<i>T. interdigitale</i> (4)	0.06*	0.04	-	Yes	
						<i>T. rubrum</i> (3)	0.5*	0.07			
						<i>T. mentagrophytes</i> (8)	16*	0.04			
8	2010	Zalacain <i>et al.</i> (8)	Spain	100	70	<i>T. rubrum</i> (35)	0.032	0.125	0.039	Yes	-
						<i>T. mentagrophytes</i> (29)	0.125	0.5	0.082		
9	2010	Beuno <i>et al.</i> (9)	Colombi a	103	30	<i>T. rubrum</i> (10)	0.03	0.06	0.026	Yes	-
						<i>T. mentagrophytes</i> (18)	0.015	0.03	0.014		
10	2009	Rodrigues <i>et al.</i> (10)	Brazil	60	60	<i>T. rubrum</i> (27)	0.125	0.25	-	-	Yes
						<i>T. mentagrophytes</i> (14)	0.06	0.25	-		
11	2007	da Silva <i>et al.</i> (11)	Brazil	100	100	<i>T. rubrum</i> (50)	<0.00 7	0.007	-	Yes	-
						<i>T. mentagrophytes</i> (50)	0.007	0.015			
12	2007	Singh <i>et al.</i> (12)	Canada	63	63	<i>T. rubrum</i> (16)	-	0.006*	-	-	Yes
						<i>T. mentagrophytes</i> (16)	-	0.004*			
13	2006	Barros <i>et al.</i> (13)	Brazil	100	100	<i>T. rubrum</i> (50)	-	0.007- 0.031#	-	Yes	-
						<i>T. mentagrophytes</i> (50)	-	<0.007 -0.015#	-		

14	2005	Esteban <i>et al.</i> (14)	Spain	59	59	<i>T. rubrum</i> (10)	0.007	0.01	0.008	-	Yes
							8				
						<i>T. mentagrophytes</i> (9)	0.01	0.03	0.015		
15	2004	Karaca <i>et al.</i> (15)	Turkey	56	56	<i>T. rubrum</i> (50)	0.002	0.008	0.02	-	Yes
							0.001	-	0.001		
						<i>T. mentagrophytes</i> (3)					

\* Minimum inhibitory concentration in µg/ml, # Range of Minimum inhibitory concentration in µg/ml, AFST= Antifungal susceptibility testing, GM= geometric mean

## References

1. Yamada T, Maeda M, Alshahni MM, Tanaka R, Yaguchi T, Bontems O, Salamin K, Fratti M, Monod M. 2017. Terbinafine resistance of *Trichophyton* clinical isolates caused by specific point mutations in the squalene epoxidase gene. *Antimicrob Agents Chemother* 61.
2. Baghi N, Shokohi T, Badali H, Makimura K, Rezaei-matehkolaei A, Abdollahi M, Didehdar M, Haghani I, Abastabar M. 2016. In vitro activity of new azoles luliconazole and lanoconazole compared with ten other antifungal drugs against clinical dermatophyte isolates 1–7.
3. Mohd Nizam T, Binting RAA, Mohd Saari S, Kumar TV, Muhammad M, Satim H, Yusoff H, Santhanam J. 2016. In Vitro Antifungal Activities against Moulds Isolated from Dermatological Specimens. *Malays J Med Sci* 23:32–9.
4. Ansar A, Farshchian M, Nazeri H, Ghiasian SA. 2011. Clinico-epidemiological and mycological aspects of tinea incognito in Iran: A 16-year study. *Japanese J Med Mycol* 52:25–32.
5. Adimi P, Hashemi SJ, Mahmoudi M, Mirhendi H, Shidfar MR, Emmami M, Rezaei-Matehkolaei A, Gramishoar M, Kordbacheh P.

2013. In-vitro Activity of 10 Antifungal Agents against 320 Dermatophyte Strains Using Microdilution Method in Tehran. Iran J Pharm Res IJPR 12:537–45.
6. Silva LB, de Oliveira DBC, da Silva B V, de Souza RA, da Silva PR, Ferreira-Paim K, Andrade-Silva LE, Silva-Vergara ML, Andrade AA. 2014. Identification and antifungal susceptibility of fungi isolated from dermatomycoses. J Eur Acad Dermatol Venereol 28:633–40.
  7. Magagnin CM, Stopiglia CDO, Vieira FJ, Heidrich D, Machado M, Vettoratto G, Lamb FM, Scroferneker ML. Antifungal susceptibility of dermatophytes isolated from patients with chronic renal failure. An Bras Dermatol 86:694–701.
  8. Zalacain A, Obrador C, Martinez JP, Viñas M, Vinuesa T. 2010. Characterization of the antimicrobial susceptibility of fungi responsible for onychomycosis in Spain. Med Mycol 49:1–5.
  9. Bueno JG, Martinez C, Zapata B, Sanclemente G, Gallego M, Mesa a C. 2010. In vitro activity of fluconazole, itraconazole, voriconazole and terbinafine against fungi causing onychomycosis. Clin Exp Dermatol 35:658–63.
  10. Rodrigues C, Mota A, Miranda KC, Lemos JDA, Costa CR, Kioko L, Passos XS, Meneses H, Rodrigues R. 2009. Comparison of in vitro activity of five antifungal agents against dermatophytes, using the agar dilution and broth microdilution methods. Rev da Soc Bras Med Trop 42:250–254.
  11. da Silva Barros ME, de Assis Santos D, Hamdan JS. 2007. Evaluation of susceptibility of *Trichophyton mentagrophytes* and *Trichophyton rubrum* clinical isolates to antifungal drugs using a modified CLSI microdilution method (M38-A). J Med Microbiol 56:514–8.
  12. Singh J, Singh J, Zaman M, Gupta AK. 2007. Evaluation of microdilution and disk diffusion methods for antifungal susceptibility testing of dermatophytes. Med Mycol 45:595–602.
  13. Barros ME da S, Santos D de A, Hamdan JS. 2006. In vitro methods for antifungal susceptibility testing of *Trichophyton* spp. Mycol Res 110:1355–60.
  14. Esteban A, Abarca ML, Cabañes FJ. 2005. Comparison of disk diffusion method and broth microdilution method for antifungal susceptibility testing of dermatophytes. Med Mycol 43:61–6.

15. Karaca N, Koç AN. 2004. In vitro susceptibility testing of dermatophytes: comparison of disk diffusion and reference broth dilution methods. *Diagn Microbiol Infect Dis* 48:259–64.

