Letter to the Editor
Clinical Microbiology

Ann Lab Med 2018;38:487-489
https://doi.org/10.3343/alm.2018.38.5.487
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

Performance of Microflex LT Biotyper and VITEK MS for Routine Identification of Yeasts

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Dear Editor,

The epidemiology of yeast infections is rapidly evolving, leading to the emergence of uncommon yeasts [1]. Rapid identification, followed by appropriate antimicrobial therapy, is associated with lower mortality [2]. Conventional phenotypic methods cannot differentiate certain yeast species accurately [3]. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) has been introduced in clinical microbiology to facilitate rapid yeast identification [3]. MALDI-TOF MS for yeast identification requires special preparation, similar to that for *Mycobacterium* species and gram-positive bacteria [4]. We compared the yeast identification capabilities of two MALDI-TOF systems—the Microflex LT Biotyper (Bruker Daltonics, Leipzig, Germany) and the VITEK MS (bioMerieux, Marcy-l'Étoile, France)—with respect to different sample preparation methods.

We included 208 yeast isolates collected from clinical samples at Severance Hospital between 2012 and 2015: blood (N=169), catheter (N=19), urine (N=12), sputum (N=6), and pus (N=2). Yeasts were identified at isolation by conventional phenotypic methods, including the VITEK 2 YST card (bioMerieux, Durham, NC, USA). For the Biotyper analysis, on-plate formic acid extraction and in-tube formic acid/acetonitrile extraction were performed as previously described [5]. For the VITEK MS, only on-plate formic acid extraction was performed because the in-tube method is not recommended by the manufacturer. When the yeast identification results of the VITEK 2 YST card and the two MALDI-TOF systems were consistent, they were considered reference identification. However, when the commercial system failed to identify the species or in cases of discordant results between the two MALDI-TOF systems, internal transcribed spacer (ITS) region sequencing was performed. This study was approved by the Institutional Review Board of Severance Hospital (2017-2752-001).

The Biotyper identification results for the two sample preparation methods are shown in Table 1. With the on-plate method, 95.7% of the isolates were correctly identified at the species level. With the in-tube extraction method, all isolates were correctly identified at the species level, consistent with previous reports [5-8]. The difference could be attributed to the ineffective lysis of the encapsulated yeast by the incomplete on-plate extraction method [9].

The Biotyper provides a species log score. A score ≥2.0 indicates excellent identification at the species level. However, the data demonstrated correct identification of isolates with cut-off scores <2.0 as well. We derived an optimal cut-off score of ≥1.7 for the Biotyper, using a ROC curve. This cut-off score demonstrated a sensitivity of 100.0% (95% confidence interval [CI] 86.3–100.0%) and a specificity of 99.5% (95% CI 98.1–99.9%).

Received: November 2, 2017
Revision received: February 20, 2018
Accepted: April 26, 2018

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Table 1. Microflex LT Biotyper identification scores using the on-plate and in-tube formic acid extraction methods

Reference ID* (N tested)	N (%) of isolates with Biotyper score									
	On-plate method						In-tube extraction method			
	≥2.0	1.9–<2.0	1.8–<1.9	1.7–<1.8	<1.7	No ID	≥2.0	1.9–<2.0	1.8–<1.9	1.7–<1.8
Candida spp.										
Candida albicans (65)	34 (52.3)	25 (38.5)	3 (4.6)	3 (4.6)			65 (100)			
Candida tropicalis (38)	8 (21.1)	15 (39.5)	11 (28.9)	1 (2.6)		3 (7.9)	35 (92.1)	3 (7.9)		
Candida glabrata (37)	28 (75.7)	4 (10.8)	3 (8.1)	1 (2.7)	1 (2.7)		37 (100)			
Candida parapsilosis (29)	4 (13.8)	9 (31)	10 (34.5)	4 (13.8)		2 (6.9)	15 (51.7)	8 (27.6)	4 (13.8)	2 (6.9)
Candida krusei (9)	7 (77.8)	1 (11.1)				1 (11.1)	7 (77.8)	2 (22.2)		
Candida lusitaniae (7)	4 (57.1)	2 (28.6)	1 (14.3)				6 (85.7)	1 (14.3)		
Candida guilliermondii (5)	3 (60)	2 (40)					4 (80)	1 (20)		
Candida dubliniensis (3)	1 (33.3)	2 (66.7)					2 (66.7)	1 (33.3)		
Candida kefyr (2)	2 (100)						2 (100)			
Non-*Candida* spp.										
Cryptococcus neoformans (6)	3 (50)		1 (16.7)			2 (33.3)	6 (100)			
Trichosporon asahii (4)	3 (75)					1 (25)	4 (100)			
Cryptococcus gattii (1)	1 (100)						1 (100)			
Cyberlindnera fabianii (1)	1 (100)						1 (100)			
Saccharomyces cerevisiae (1)	1 (100)						1 (100)			
Total (208)	100 (48.1)	60 (28.8)	29 (13.9)	9 (4.3)	1 (0.5)	9 (4.3)	186 (89.4)	16 (7.7)	4 (1.9)	2 (1)
Cumulative Total	100 (48.1)	160 (76.9)	189 (90.8)	198 (95.2)	199 (95.7)	208 (100)	186 (89.4)	202 (97.1)	206 (99.0)	208 (100)

*If the identifications of the three methods were consistent, the result was considered a reference identification. When any of the results varied, ITS region sequencing was performed.
Abbreviation: ID, identification.

Table 2. Identification of clinical yeast isolates using the Microflex LT Biotyper, VITEK MS, and VITEK 2

Reference ID (N, ITS-tested N)	Microflex LT Biotyper		VITEK MS		VITEK 2	
	Correct IDs at the species level	Discordant IDs	Correct IDs at the species level	Discordant IDs	Correct IDs at the species level	Discordant IDs
Candida albicans (65, 1)	65 (100)		65 (100)		64 (98.5)	1 (1.5)
Candida tropicalis (38, 1)	37 (100)		37 (100)		37 (97.4)	1 (2.6)
Candida glabrata (37, 0)	37 (100)		37 (100)		37 (100)	
Candida parapsilosis (29, 3)	29 (100)		29 (100)		24 (82.8)	5 (17.2)
Candida krusei (9, 1)	9 (100)		9 (100)		7 (77.8)	2 (22.2)
Candida lusitaniae (7, 2)	7 (100)		7 (100)		5 (71.4)	2 (28.6)
Candida guilliermondii (5, 3)	5 (100)		5 (100)		1 (20.0)	4 (80.0)
Candida dubliniensis (3, 1)	3 (100)		3 (100)		2 (66.7)	1 (33.3)
Candida kefyr (2, 0)	2 (100)		2 (100)		2 (100)	
Cryptococcus neoformans (6, 1)	6 (100)		6 (100)		5 (83.3)	1 (16.7)
Trichosporon asahii (4, 1)	4 (100)		4 (100)		3 (75.0)	1 (25.0)
Cryptococcus gattii (1, 1)	1 (100)		0 (0)	1 (100)		1 (100)
Cyberlindnera fabianii (1, 1)	1 (100)		1 (100)			1 (100)
Saccharomyces cerevisiae (1, 0)	1 (100)		1 (100)		1 (100)	
Total (208, 20)	208 (100)		207 (99.5)	1 (0.5)	188 (90.4)	20 (9.6)

Values are presented as N (%).
Abbreviations: ID, identification; ITS, internal transcribed spacer; MS, mass spectrometry.

https://doi.org/10.3343/alm.2018.38.5.487

When this cut-off was applied, 94.7% of the isolates were correctly identified at the species level using the Biotyper system with the on-plate method. This rate increased to 100% using the same system with the in-tube method. With this cut-off, the yeast identification ability of the Biotyper was comparable with that of VITEK MS. The final identification rates were 100.0% and 99.5% for the Biotyper and VITEK MS, respectively (Table 2). VITEK MS provided correct identification at the species level for all 208 isolates, except *Cryptococcus gattii*, which is not included in the VITEK MS database. The correct identification rate of the VITEK 2 system with the YST card was 90.4%.

Previous studies have suggested various cut-off values <2 [3, 10], and we found that the laboratory-validated cut-off value yielded a higher identification rate without compromising accuracy. Lee *et al* [5] reported correct identification rates of 91.4% and 97.8% using the Biotyper (≥1.7) and the VITEK MS, respectively, with the on-plate method. Their results included 37 uncommon yeast species, which might explain why their correct identification rates were slightly lower than ours (94.7% and 99.5%).

The on-plate method is preferred to in-tube extraction method. The latter method is time-consuming and laborious, although, traditionally, it has provided better identification results in the clinical laboratory. Lower cut-off scores using the on-plate method have resulted in greater consistency between the results of the two methods, except for *C. neoformans*. Moreover, the on-plate method may reduce the time and labor required to perform retests that are often required with the in-tube method or other complementary tests, such as ITS region sequencing.

In summary, the Biotyper and VITEK MS platforms demonstrated comparable performance for routine identification of clinically common yeasts (100% vs 99.5%, respectively). VITEK MS yields accurate results using the simple on-plate method. The Biotyper requires the in-tube extraction method to reach a score ≥2.0; however, with the application of a flexible cut-off value (≥1.7), the on-plate method is sufficient to achieve a correct identification rate of >95%.

Authors' Disclosure of Potential Conflict of Interest

No potential conflicts of interest relevant to this article were reported.

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