

**A MULTI-SCREENING APPROACH FOR MARINE-DERIVED FUNGAL METABOLITES AND THE ISOLATION OF CYCLODEPSIPEPTIDES FROM *Beauveria felina***

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**Table 1S.** Identification\*, origin and growth media of the 57 strains of marine fungi, as well as the growth mode of marine-derived fungal strains which yielded crude extracts with a distinctive chemical profile analyzed by HPLC-PDA and TLC

Fungi strain	Origin	MF Culture medium		Growth mode	HPLC-PDA distinctive (# of peaks)	TLC (Dragendorff)
		saline	salt-free			
Unidentified fungus <b>S4SS1</b>	Sediment	+	-			
<i>Hansfordia ovalispora</i> <b>S4SS2</b>	Sediment	+	+	D	+ (1)	-
Unidentified fungus <b>AbSS3</b>	<i>Padina</i> sp.	+	-			
<i>Phoma</i> sp. 1 <b>S2SS4</b>	Sediment	+	+	D	+ (1)	+
Unidentified fungus <b>S3SS5</b>	Sediment	+	-	D	+ (2)	+
Unidentified fungus <b>S4SS6</b>	Sediment	+	-	D	+ (1)	-
<i>Spadicoides</i> sp. 1 <b>S4SS7</b>	Sediment	+	-	D	+ (1)	-
<i>Beauveria felina</i> <b>AcSS8</b>	<i>Caulerpa</i> sp.	+	+	D	+ (1)	-
Unidentified fungus <b>AcSS9</b>	<i>Caulerpa</i> sp.	+	+	D	+ (1)	-
Unidentified fungus <b>AcSS10</b>	<i>Caulerpa</i> sp.	+	+			
Unidentified fungus <b>S4SS11</b>	Sediment	+	+			
<i>Rhinoctadiella</i> sp. <b>AcSS12</b>	<i>Caulerpa</i> sp.	+	-	S	+ (1)	-
<i>Beauveria felina</i> <b>AcSS13</b>	<i>Caulerpa</i> sp.	+	+	D	-	+
<i>Phoma</i> sp. 2 <b>AcSS14</b>	<i>Caulerpa</i> sp.	+	-			
<i>Rhinoctadiella</i> sp. 2 <b>Ad(SS)P15</b>	Unidentified algae	+	-	D	-	+
<i>Penicillium</i> sp. 1 <b>S2SS16</b>	Sediment	+	+	S	+ (1)	-
Unidentified fungus <b>AaSS17</b>	<i>Sargassum cymosum</i>	+	+	S	-	+
Unidentified fungus <b>CSS18</b>	<i>Anemonia sargassensis</i>	+	+			
<i>Penicillium</i> sp. 2 <b>CSS19</b>	<i>Anemonia sargassensis</i>	+	+	S	+ (1)	-
Unidentified fungus <b>S2SS20</b>	Sediment	+	-			
<i>Penicillium</i> sp. 3 <b>S1SS21</b>	Sediment	+	+			
<i>Spadicoides</i> sp. <b>AbSS22</b>	<i>Padina</i> sp.	+	+			
Unidentified fungus <b>S1SS23</b>	Sediment	+	+	D	-	+
Unidentified fungus <b>S2SS24</b>	Sediment	+	+			

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**Table 1S.**

Fungi strain	Origin	MF Culture medium		Growth mode	HPLC-PDA distinctive (# of peaks)	TLC (Dragendorff)
		saline	salt-free			
Unidentified fungus <b>S1SS25</b>	Sediment	+	+	S	-	+
<i>Curvularia borrieriae</i> <b>RP26</b>	Rock	+	+			
Unidentified fungus <b>AaSS27</b>	<i>Sargassum cymosum</i>	+	+	S	-	+
Unidentified fungus <b>S1SS28</b>	Sediment	+	-			
<i>Penicillium</i> sp. 4 <b>AbSS29</b>	<i>Padina</i> sp.	+	+			
<i>Penicillium</i> sp. 1 <b>S1SS30</b>	Sediment	+	+			
Unidentified fungus <b>S1SS31</b>	Sediment	+	+	D	+ (1)	-
Unidentified fungus <b>S3SS32</b>	Sediment	+	+	S	-	+
Unidentified fungus <b>S2SS33</b>	Sediment	+	+			
Unidentified fungus <b>S1SS34</b>	Sediment	+	+	S	-	+
Unidentified fungus <b>AaSS35</b>	<i>Sargassum cymosum</i>	+	-			
<i>Verticillium</i> sp. 2 <b>AaSS36</b>	<i>Sargassum cymosum</i>	+	+			
Unidentified fungus <b>CSS37</b>	<i>Anemonia sargassensis</i>	+	+			
<i>Verticillium</i> sp. 3 <b>S3SS38</b>	Sediment	+	+	S	+ (2)	-
<i>Verticillium</i> sp. 4 <b>SP39</b>	Sediment	+	+			
<i>Spadicoides</i> sp. 2 <b>AbSS40</b>	<i>Padina</i> sp.	+	+	S	+ (2)	-
<i>Penicillium</i> sp. 5 <b>ESS41</b>	<i>Tedania ignis</i>	+	+	S	+ (4)	-
<i>Penicillium</i> sp. 6 <b>AbSS42</b>	<i>Padina</i> sp.	+	+			
<i>Aspergillus</i> sp. 1 <b>SP43</b>	Sediment	+	-			
<i>Aspergillus</i> sp. 2 <b>SP44</b>	Sediment	+	+			
<i>Penicillium</i> sp. 7 <b>RP45</b>	Rock	+	+			
Unidentified fungus <b>AbSS46</b>	<i>Padina</i> sp.	+	+			
Unidentified fungus <b>SP47</b>	Sediment	+	+	S	+ (2)	-
Unidentified fungus <b>RP48</b>	Rock	+	-			
Unidentified fungus <b>RP49</b>	Rock	+	+			
Unidentified fungus <b>SP50</b>	Sediment	+	+	S	+ (1)	-
Unidentified fungus <b>SP50</b>	Sediment	+	+	D	+ (1)	-
<i>Pestalotiopsis</i> sp. 1 <b>SP51</b>	Sediment	+	+	S	+ (2)	+
<i>Verticillium</i> sp. 5 <b>AcSS52</b>	<i>Caulerpa</i> sp.	+	+			
<i>Penicillium</i> sp. <b>AcSS53</b>	<i>Caulerpa</i> sp.	+	+	S	+ (4)	-
<i>Penicillium</i> sp. 8 <b>AcSS54</b>	<i>Caulerpa</i> sp.	+	+	S	+ (3)	-
<i>Pestalotiopsis</i> sp. 2 <b>SP55</b>	Sediment	+	-			
Unidentified fungus <b>SP56</b>	Sediment	+	+	S	-	+
Unidentified fungus <b>AaSS57</b>	<i>Sargassum cymosum</i>	+	+			

\*Alpha-numerical codes refer to the authors fungal sample repository, where voucher samples of all fungal strains have been deposited; D: growth in dynamic mode with shaking at 200 rpm ; S: growth in still mode.

**Table 2S.** Antimycobacterial, antibiotic, antifungal and cytotoxic activities of crude extracts obtained from marine fungi strains

FUNGI STRAIN	GROWTH MODE	MICROORGANISMS													cell lines		
		1	2	3	4	5	6	7	8	9	10	11	12	13	A	B	C
S4SS2	S	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-
S2SS4	S	+++	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
S3SS5	D	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
S4SS6	D	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AcSS8	D	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	S	++	-	-	-	-	-	-	-	-	-	-	-	-	++	+++	++
AcSS9	S	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
AcSS12	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+
AcSS13	D	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+
	S	++	-	-	-	-	-	-	-	-	-	-	-	-	+	+++	++
AdP15	S	-	-	-	-	-	-	-	-	-	-	-	-	-	+	++	++
S2SS16	S	-	-	-	-	-	-	-	-	-	-	-	++	-	-	+	++
CSS19	D	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
	S	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+++
AbSS22	D	+	-	-	-	-	-	-	-	+	++	-	-	-	-	-	-
S1SS23	D	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
S2SS24	D	-	-	-	-	+++	-	-	-	-	-	-	-	-	-	-	-
	S	-	-	-	-	-	-	-	-	-	-	-	-	-	++	++	++
S1SS25	S	++	-	-	-	-	-	-	-	-	-	-	-	-	-	++	+
RP26	D	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-
S1SS28	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
AbSS29	D	++	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
S1SS30	S	+++	-	-	-	-	-	-	-	-	-	-	-	-	+	+++	+++
S1SS31	S	-	-	-	-	-	-	-	-	-	-	-	-	-	+	++	+++
S3SS32	S	-	-	-	-	-	-	+	-	+	-	-	-	-	-	+	+
S2SS33	S	++	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
AaSS35	D	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
S3SS38	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+
SP43	D	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
SP44	D	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-
RP45	D	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-
AbSS46	D	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
SP47	S	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
RP49	D	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-
AcSS52	S	-	-	-	-	+	-	-	-	-	-	-	-	+++	-	-	-
AcSS53	S	-	-	-	-	+	-	-	-	-	-	-	-	+++	-	-	-
AcSS54	D	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-
SP55	D	+++	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SP56	S	+++	-	-	+	-	-	-	-	-	-	-	-	+++	-	-	+
AaSS57	D	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-

Growth mode: D: dynamic (stirring at 200 rpm); S: still. Microorganism strains: **1:** *M. tuberculosis*; **2:** *P. aeruginosa* ATCC 27583; **3:** *E. coli* (antibiotic resistant); **4:** *E. coli* ATCC 25922; **5:** *S. aureus* ATCC 25923; **6:** *S. aureus* resistant strain #8; **7:** *S. aureus* resistant strain #18; **8:** *S. aureus* resistant strain #115; **9:** *S. aureus* resistant strain #134; **10:** *E. faecalis* ATCC 29212; **11:** *S. choleraesuis* ATCC 10708; **12:** *E. cloacae* resistant strain #19; **13:** *C. albicans* ATCC 10231; Tumor cell lines **A:** MCF-7 (breast); **B:** HCT-8 (colon); **C:** B16 (murine melanoma). Antibacterial activity level: + inhibition zone >10 mm and < 14 mm; ++ inhibition zone > 15 mm and < 20 mm; +++ inhibition zone > 20 mm, except for *M. tuberculosis*. Antimycobacterial activity level against *M. tuberculosis*: +++ inhibition at 31.25 µg/mL; ++ inhibition at 62.5 µg/mL; + inhibition at 125 µg/mL. Antiproliferative activity level: + inhibition up to 50% of cancer cell growth; ++ inhibition between 50 and 75% of cancer cell growth; +++ inhibition larger than 75% of cell growth. – Not active.

**Table 3S.** Number of crude extracts obtained from marine fungal strains that displayed distinctive chemical profiles and biological activities

Fungi strains		PDA-HPLC	TLC	Antibacterial	Antifungal	Cytotoxic
Growth mode	still	11	7	14	3	15
	dynamic	9	5	18	0	1
Origin	sediments	12	8	19	1	9
	algae	6	4	12	2	5
	sponge	1	0	0	0	0
	cnidarian	1	0	1	0	1

**Table 4S.** Number of crude extracts obtained from marine-derived fungi that presented simultaneously two or three chemical profile and/or biological activities

Biological activities		(1) + (2)	(1) + (3)	(1) + (4)	(1) + (5)	(2) + (3)	(2) + (4)	(2) + (5)	(3) + (4)	(3) + (5)	(1) + (2) + (3)	(2) + (3) + (4)	(2) + (4) + (5)	(3) + (4) + (5)
Fungi	still	1	3	1	3	3	1	3	3	7	0	1	1	1
Growth mode	dynamic	2	3	0	0	1	0	1	0	0	1	0	0	0
Fungi	sediments	2	4	0	1	4	1	3	1	5	1	1	1	1
Origin	algae	0	2	1	1	0	0	1	2	2	0	0	0	0
	sponge	0	0	0	0	0	0	0	0	0	0	0	0	0
	cnidarian	0	0	0	1	0	0	0	0	0	0	0	0	0

Legend: (1): distinctive HPLC-PDA chemical profile (chromatograms with peaks which displayed UV absorptions with  $\lambda_{\max}$  above 250 nm); (2) Alkaloids present (Dragendorff positive in TLC analysis); (3) Antibacterial positive; (4) Antifungal positive; (5) Cytotoxic positive.