

***Syngysium jambos* displayed antibacterial and antibiotic-modulating activities against resistant phenotypes**

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Table S1. *Staphylococcus aureus* strains and features

Bacteria	Features	References
<i>S. aureus</i> MSSA1	Clinical isolate : Met susceptible ; Nis ^r , Chl ^r	[1, 2]
<i>S. aureus</i> MRSA3	Clinical isolate : Ofxa ^r , Kan ^r , Tet ^r , Erm ^r	[1]
<i>S. aureus</i> MRSA4	Clinical isolate : Ofxa ^r , Kan ^r , Cyp ^r , Chl ^r , Gen ^r , Nis ^r , Amp ^r	[1, 2]
<i>S. aureus</i> MRSA6	Clinical isolate : Ofxa ^r , Flx ^r , Kan ^r , Tet ^r , Cyp ^r , Im/Cs ^r , Chl ^r , Gen ^r , Nis ^r , Amp ^r	[1, 2]
<i>S. aureus</i> MRSA8	Clinical isolate : Ofxa ^r , Flx ^r , Kan ^r , Erm ^r , Cyp ^r , Im/Cs ^r , Chl ^r , Gen ^r , Nis ^r , Amp ^r	[1, 2]
<i>S. aureus</i> MRSA9	Clinical isolate : Ofxa ^r , Flx ^r , Tet ^r , Erm ^r , Cyp ^r , Im/Cs ^r , Chl ^r , Gen ^r , Nis ^r , Amp ^r	[1, 2]
<i>S. aureus</i> MRSA11	Clinical isolate : Ofxa ^r , Kan ^r , Erm ^r , Cyp ^r , Im/Cs ^r , Chl ^r , Nis ^r , Amp ^r	[1, 2]
<i>S. aureus</i> MRSA12	Clinical isolate : Ofxa ^r , Flx ^r , Kan ^r , Erm ^r , Im/Cs ^r , Chl ^r , Gen ^r , Nis ^r , Amp ^r	[1, 2]
ATCC 25923	Reference strain	/
SA01	Clinical isolate : Erm ^r , Amp ^r	[3]
SA07	Clinical isolate : Erm ^r , Dox ^r	[3]
SA18	Clinical isolate : Amp ^r , Dox ^r , Vm ^r	[3]
SA23	Clinical isolate : Imi ^r , Aug ^r	[3]
SA36	Clinical isolate : Dox ^r , Vm ^r	[3]
SA39	Clinical isolate : Amp ^r	[3]
SA56	Clinical isolate : Amp ^r , Dox ^r	[3]
SA64	Clinical isolate : Amp ^r , Dox ^r	[3]
SA68	Clinical isolate : Amp ^r , Vm ^r	[3]
SA88	Clinical isolate : Erm ^r , Vm ^r	[3]
SA114	Clinical isolate : Amp ^r , Dox ^r	[3]
SA116	Clinical isolate : Erm ^r	[3]
SA124	Clinical isolate : Erm ^r	[3]
SA126	Clinical isolate : Amp ^r , Dox ^r	[3]
SA127	Clinical isolate : Amp ^r , Dox ^r	[3]
SA135	Clinical isolate : Erm ^r	[3]
SA139	Clinical isolate : Erm ^r	[3]

Chl^r, Cyp^r, Erm^r, Flx^r, Im/Cs^r, Kan^r, Met^r, Ofxa^r, Tet^r, Vm^r, Amp^r, Dox^r, Aug^r, Gen^r and Nis^r résistance to : chloramphenicol; Cyprofloxacin; Erythromycin; Flomoxef; Imipenem/CilaSAatin sodium; Kanamycin; Méthicillin; Ofloxacin; Tetracycline; Vancomycin ; Ampicillin ; Doxycycline ; Augmentin ; Gentamicin ; Nisin respectively, SA : *SAaphyococcus aureus*.

Table S2. Gram-negative bacteria and features

Strains	Features and References
<i>Escherichia coli</i>	
ATCC8739	Reference strain
AG100	Wild-type <i>E. coli</i> K-12 [4]
AG100 _{A^{TET}}	Δ <i>acrAB</i> mutant AG100, with over-expressing <i>acrF</i> gene ; TET ^R [4]
AG102	Δ <i>acrAB</i> mutant AG100, owing <i>acrF</i> gene markedly over-expressed; TET ^R [5, 6]
MC4100	Wild type <i>E. coli</i> [7]
<i>Enterobacter aerogenes</i>	
ATCC13048	Reference strains
CM64	CHL ^R resistant variant obtained from ATCC13048 over-expressing the AcrAB pump [8]
EA3	Clinical MDR isolate; CHL ^R , NOR ^R , OFX ^R , SPX ^R , MOX ^R , CFT ^R , ATM ^R , FEP ^R [9, 10]
EA27	Clinical MDR isolate exhibiting energy-dependent norfloxacin and chloramphenicol efflux with KAN ^R AMP ^R NAL ^R STR ^R TET ^R [9, 10]
EA289	KAN sensitive derivative of EA27 [11]
EA294	EA289 <i>acrA</i> ::KAN ^R [11]
EA298	EA 289 <i>tolC</i> ::KAN ^R [11]
<i>Enterobacter cloacae</i>	
ECCI69	Clinical MDR isolates, CHL ^R [12]
<i>Klebsiella pneumoniae</i>	
ATCC12296	Reference strains
KP55	Clinical MDR isolate, TET ^R , AMP ^R , ATM ^R , CEF ^R [13]
KP63	Clinical MDR isolate, TET ^R , CHL ^R , AMP ^R , ATM ^R [13]
K24	AcrAB-TolC, Laboratory collection of UNR-MD1, University of Marseille, France [12]
<i>Providencia stuartii</i>	
NEA16	Clinical MDR isolate, AcrAB-TolC
PS299645	Clinical MDR isolate, AcrAB-TolC [14]
<i>Pseudomonas aeruginosa</i>	
PA 01	Reference strains
PA 124	MDR clinical isolate [15]

^aAMP, ATM^R, CEF^R, CFT^R, CHL^R, FEP^R, KAN^R, MOX^R, OFX^R, STR^R, TET^R. Resistance to ampicillin, aztreonam, cephalothin, cefadroxil, chloramphenicol, cefepime, kanamycin, moxalactam, ofloxacin, streptomycin, and tetracycline; MDR : Multidrug resistant; AcrAB-TolC efflux pump AcrAB associate to TolC porin,

References

1. A. Paudel, H. Hamamoto, Y. Kobayashi, S. Yokoshima, T. Fukuyama, and K. Sekimizu. "Identification of novel deoxyribofuranosyl indole antimicrobial agents," *J Antibiot (Tokyo)*, vol. 65, no. 2, pp. 53-57.
2. J.P. Dzoyem, H. Hamamoto, B. Ngameni, B.T. Ngadjui, and K. Sekimizu. "Antimicrobial action mechanism of flavonoids from *Dorstenia* species," *Drug Discov Ther*, vol. 7, no. 2, pp. 66-72.
3. T.J.O. Ngalani, [*Influence de la multi-résistance des bactéries entériques aux antibiotiques sur l'état immunologique des patients séropositifs au VIH venus en consultation à l'hôpital Adlucem Banka de Bafang*], Department of Biochemistry, University of Dschang, Cameroon, 2015.
4. M. Viveiros, A. Jesus, M. Brito, et al. "Inducement and reversal of tetracycline resistance in *Escherichia coli* K-12 and expression of proton gradient-dependent multidrug efflux pump genes," *Antimicrob Agents Chemother*, vol. 49, no. 8, pp. 3578-3582.
5. C.A. Elkins and L.B. Mullis. "Substrate competition studies using whole-cell accumulation assays with the major tripartite multidrug efflux pumps of *Escherichia coli*," *Antimicrob Agents Chemother*, vol. 51, no. 3, pp. 923-929.
6. V. Kuete, S. Alibert-Franco, K.O. Eyong, et al. "Antibacterial activity of some natural products against bacteria expressing a multidrug-resistant phenotype," *Int J Antimicrob Agents*, vol. 37, no. 2, pp. 156-161.
7. P. Baglioni, L. Bini, S. Liberatori, V. Pallini, and L. Marri. "Proteome analysis of *Escherichia coli* W3110 expressing an heterologous sigma factor," *Proteomics*, vol. 3, no. 6, pp. 1060-1065.
8. D. Ghisalberti, M. Masi, J.M. Pages, and J. Chevalier. "Chloramphenicol and expression of multidrug efflux pump in *Enterobacter aerogenes*," *Biochem Biophys Res Commun*, vol. 328, no. 4, pp. 1113-1118.
9. M. Mallea, J. Chevalier, C. Bornet, et al. "Porin alteration and active efflux: two in vivo drug resistance strategies used by *Enterobacter aerogenes*," *Microbiology*, vol. 144 (Pt 11), pp. 3003-3009.
10. M. Mallea, A. Mahamoud, J. Chevalier, et al. "Alkylaminoquinolines inhibit the bacterial antibiotic efflux pump in multidrug-resistant clinical isolates," *Biochem J*, vol. 376, no. Pt 3, pp. 801-805.
11. E. Pradel and J.M. Pages. "The AcrAB-TolC efflux pump contributes to multidrug resistance in the nosocomial pathogen *Enterobacter aerogenes*," *Antimicrob Agents Chemother*, vol. 46, no. 8, pp. 2640-2643.
12. A.G. Fankam, V. Kuete, I.K. Voukeng, J.R. Kuate, and J.M. Pages. "Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes," *BMC Complement Altern Med*, vol. 11, p. 104.
13. J. Chevalier, J.M. Pages, A. Eyraud, and M. Mallea. "Membrane permeability modifications are involved in antibiotic resistance in *Klebsiella pneumoniae*," *Biochem Biophys Res Commun*, vol. 274, no. 2, pp. 496-499.
14. Q.T. Tran, K.R. Mahendran, E. Hajjar, et al. "Implication of porins in beta-lactam resistance of *Providencia stuartii*," *J Biol Chem*, vol. 285, no. 42, pp. 32273-32281.
15. V. Lorenzi, A. Muselli, A.F. Bernardini, et al. "Geraniol restores antibiotic activities against multidrug-resistant isolates from gram-negative species," *Antimicrob Agents Chemother*, vol. 53, no. 5, pp. 2209-2211.

