Novel Organometallic Complexes with Potent Selective Antimicrobial Activity

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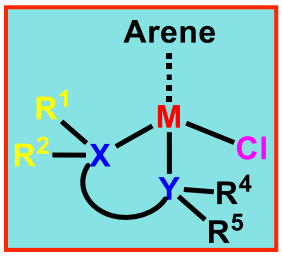
WARWICK
INTEGRATE ANTIMICROBIAL RESISTANCE

Introduction:

- Antimicrobial resistance in single organisms is unprecedented and mounting.[1]
- Developing of new effective antimicrobial agents is urgently needed to circumvent severe drug resistance.[2]
- In this project, a series of novel organometallic complexes with potent antimicrobial activity were synthesized.
- The antimicrobial activity of these complexes have been screened against a range of Gram-positive bacteria and fungi (*C. neoformans*), and cytotoxicity against Human Embryonic Kidney cell (*HEK-293*) was also investigated.

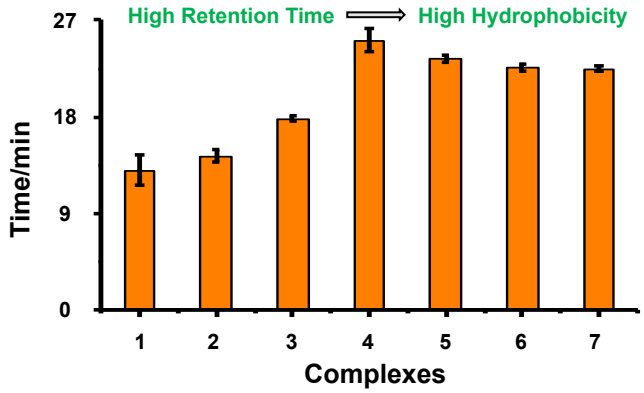
1. Synthesis of Organometallic Complexes 1-7



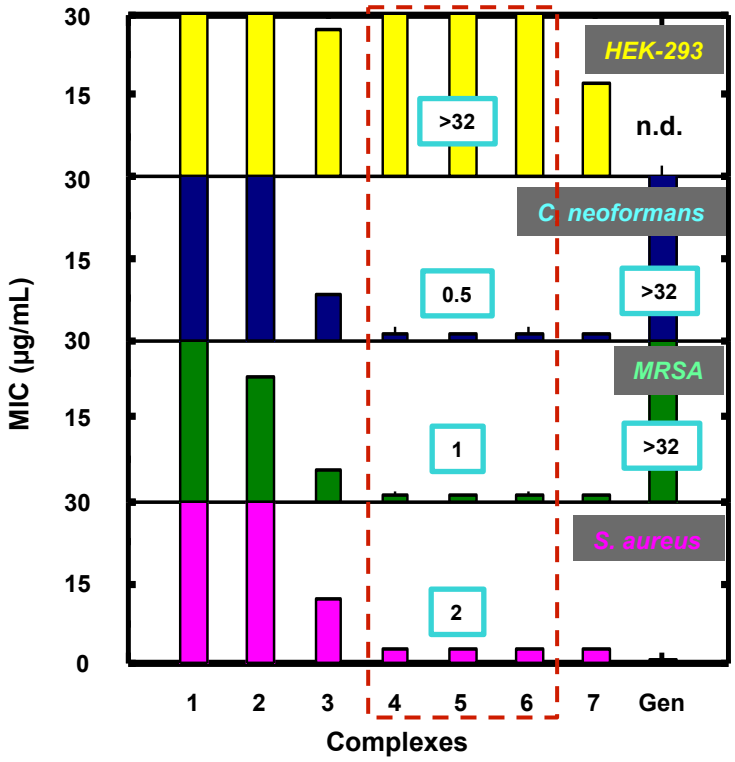
Confirmed by NMR, Mass spectra and Crystal Structures

Complex	R^1	R^2
1	-CH3	-CH3
2	-CH3	-CH3
3	-CH3	-CH3
4	H	-Benzene (Bn)
5	H	-4-F-Bn
6	H	-2-Me-Bn
7	H	-Phenethylethane

2. Retention Time of Complexes 1-7 by RP-HPLC

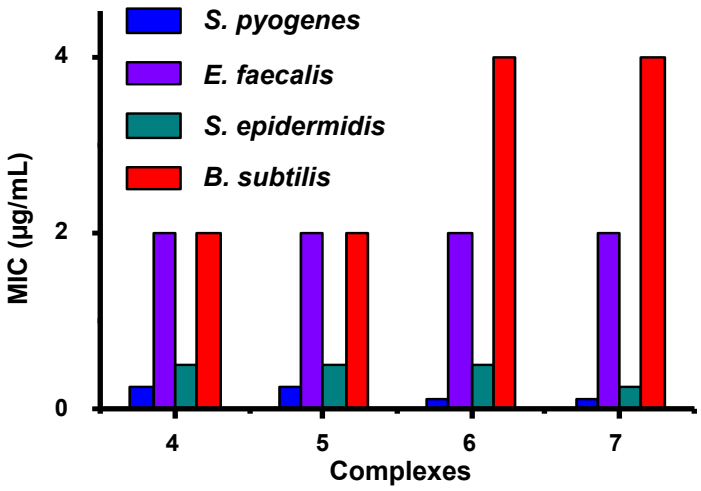


3. Antimicrobial Activity and Cytotoxicity of Complexes 1-7



MIC: minimum inhibitory concentrations; *HEK-293*: Human embryonic kidney cells; *C. neoformans*: Cryptococcus neoformans var. grubii, ATCC 208821; *MRSA*: Methillicin Resistant Staphylococcus aureus, ATCC 43300; *S. aureus*: Staphylococcus aureus, R 34. Gen: Gentamicin.

4. Antibacterial Activity (MIC) of Complexes 1-7 Against a Range of Gram-positive Bacteria



S. Pygenes: Streptococcus Pyogenes, 151112; *E. faecalis*: Enterococcus faecalis, 29212; *S. epidermidis*: Staphylococcus epidermidis, 12228; *B. subtilis*: Bacillus subtilis, DSM 10.

5. Conclusions:

- Series of organometallic complexes have been synthesized and structures have been confirmed by X-ray crystallography.
- Complexes 4-6 showed high potency against a variety of Gram-positive bacteria and also exhibited great antifungal activity towards *C. neoformans*.
- Complexes 4, 5 and 6 exhibited low toxicity against mammalian cells (human embryonic kidney cells), indicating a high selectivity and promise for future development as new antimicrobial agents to combat resistance.

6. Acknowledgements:

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7. References:

1. Levy, S. B and Marshall, B.; *Nature Medcine.* **2004,** 10, 122-129.
2. Vajs, J.; Proud, C.; Brozovic, A.; Gazvoda, M.; Lloyd, A.; Roper, D. I.; Osmak, M.; Kosmrlj, J.; Dowson, C. G., *Eur. J. Med. Chem.* **2012**, 127, 223−234.