Hospital General Universitario Gregorio Marañón

The Optimal Ethanol Lock Therapy Regimen for the Treatment of Biofilm-Associated Catheter Infections: Results From an In Vitro Study

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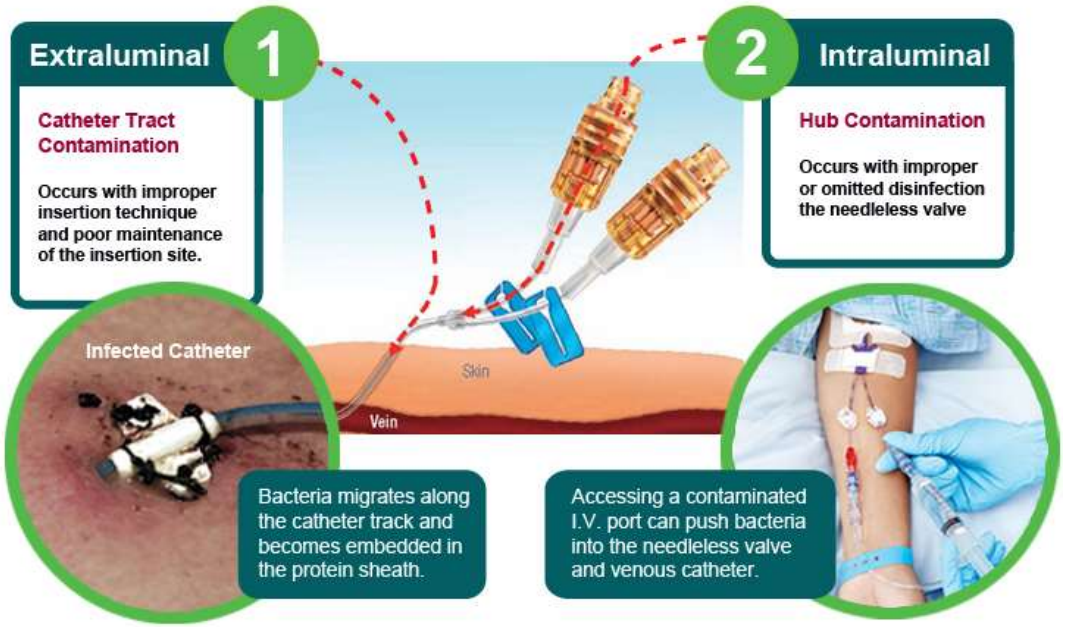
BACKGROUND

❖**Catheter-related bloodstream infection (C-RBSI)** is a major nosocomial infection[1,2].

❖C-RBSI **rates** range from 2 to 5 episodes/1,000 catheter days[1,6].

Clinical impact

- Attributable **mortality** rate: 10-15%[3].
- Extra days of **hospitalization**: 15-25[3,4].
- Associated **costs**: 18,000€ (Spain)-50,000$ (USA)[3,5].



[1] Mermel et al. Clin Infect Dis 2009.

[2] O'Grady et al. Clin Infect Dis 2011.

[3] Warren et al. Crit Care Med 2006.

[4] Shannon et al. Am J Med Qual 2016.

[5] Riu et al. Enferm Infecc Microbiol Clin. 2012.

[6] Maki et al. Mayo Clin Proc 2006.

BACKGROUND

❖Guidelines recommend **catheter withdrawal** when there is suspicion of C-RBSI (A-II)[1].

❖When catheter is esential, the combination of **systemic** antimicrobials with antimicrobial **lock therapy** is recommended (B-II)[1].

❖Long-term CVCs infection is mainly associated with intraluminal colonization ➡ Biofilm

[1] Mermel et al. Clin Infect Dis 2009

BACKGROUND

ALT

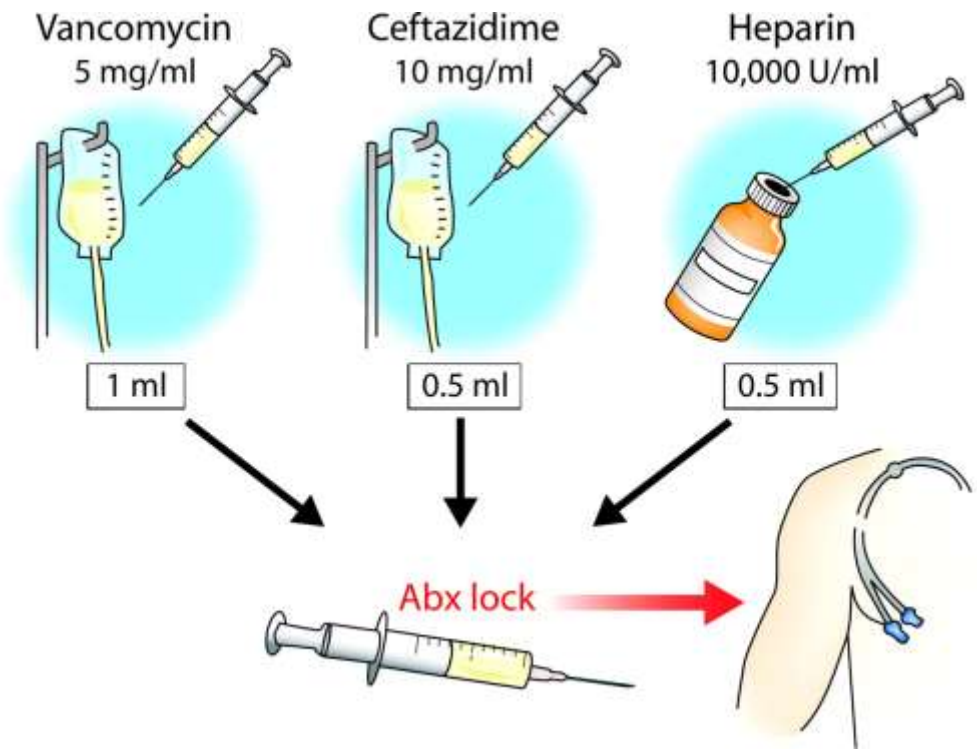
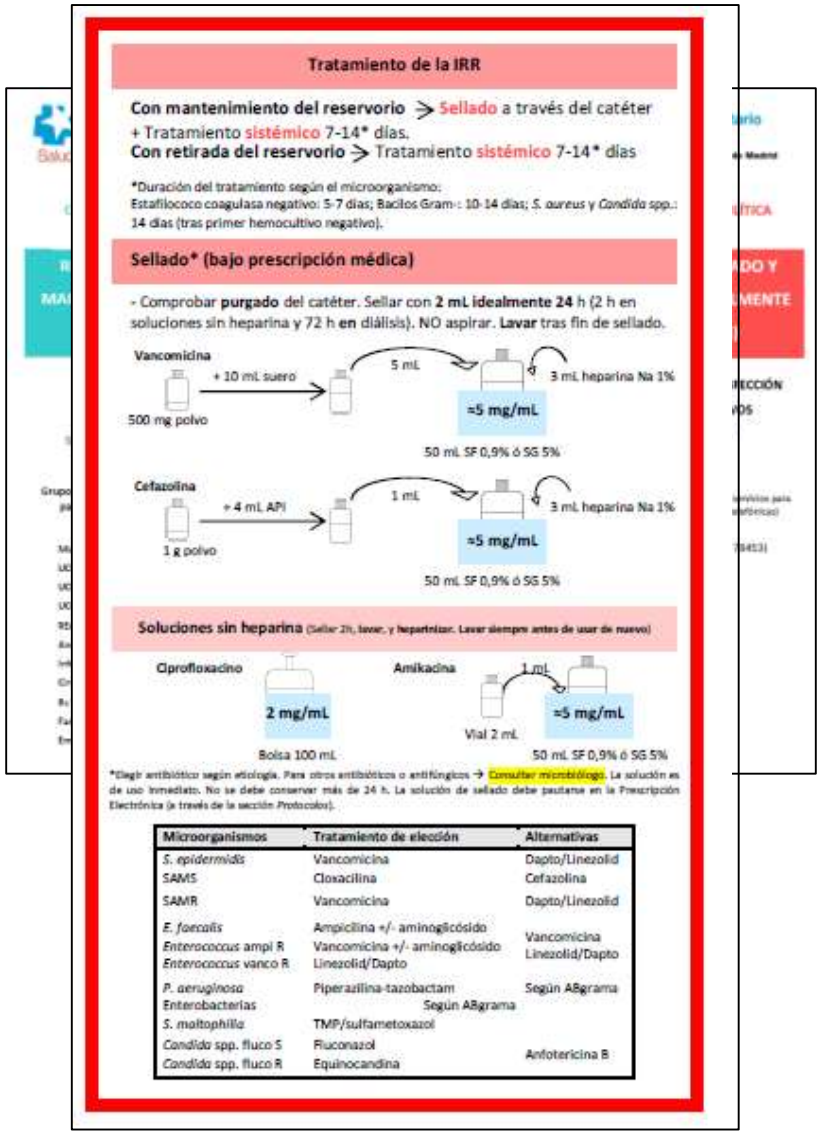


Image from the Clinical Journal of the American Society of Nephrology



Tratamiento de la IRR

Con mantenimiento del reservorio → Sellado a través del catéter
+ Tratamiento sistémico 7-14* días.
Con retirada del reservorio → Tratamiento sistémico 7-14* días

*Duración del tratamiento según el microorganismo:
Estafilococo coagulasa negativo: 5-7 días; Bacilos Gram-: 10-14 días; *S. aureus* y *Candida* spp.: 14 días (tras primer hemocultivo negativo).

Sellado* (bajo prescripción médica)

- Comprobar **purgado** del catéter. Sellar con **2 mL idealmente 24** h (2 h en soluciones sin heparina y 72 h **en** diálisis). NO aspirar. **Lavar** tras fin de sellado.

Vancomicina
+ 10 mL suero → 5 mL → 3 mL heparina Na 1%
500 mg polvo → ≈5 mg/mL
50 mL SF 0,9% ó SG 5%

Cefazolina
+ 4 mL API → 1 mL → 3 mL heparina Na 1%
1 g polvo → ≈5 mg/mL
50 mL SF 0,9% ó SG 5%

Soluciones sin heparina (Sellar 2h, lavar, y heparinizar. Lavar siempre antes de usar de nuevo)

Ciprofloxacino
2 mg/mL
Bolsa 100 mL

Amikacina
1 mL → ≈5 mg/mL
Vial 2 mL
50 mL SF 0,9% ó SG 5%

*Elegir antibiótico según etiología. Para otros antibióticos o antifúngicos → Consultar microbiólogo. La solución es de uso inmediato. No se debe conservar más de 24 h. La solución de sellado debe pautarse en la Prescripción Electrónica (a través de la sección *Protocolos*).

Microorganismos	Tratamiento de elección	Alternativas
S. epidermidis	Vancomicina	Dapto/Linezolid
SAMS	Cloxacilina	Cefazolina
SAMR	Vancomicina	Dapto/Linezolid
E. faecalis	Ampicilina +/- aminoglicósido	Vancomicina
Enterococcus ampi R	Vancomicina +/- aminoglicósido	Linezolid/Dapto
Enterococcus vanco R	Linezolid/Dapto	
P. aeruginosa	Piperacilina-tazobactam	Según ABgrama
Enterobacterias	Según ABgrama	
S. maltophilia	TMP/sulfametoxazol	
Candida spp. fluco S	Fluconazol	Anfotericina B
Candida spp. fluco R	Equinocandina	

BACKGROUND

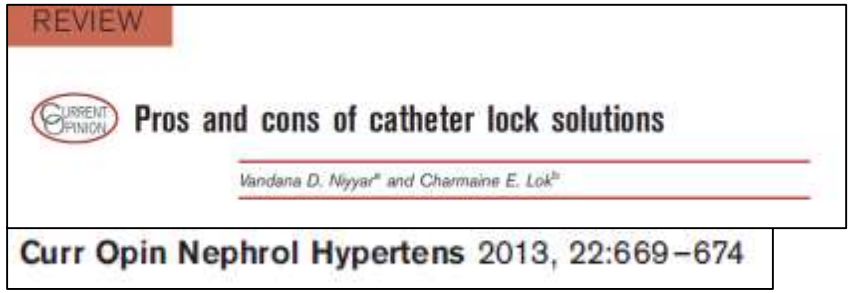
❖Alternatively, **antiseptic** lock solutions are being used.

❖Although ethanol lock therapy (**ELT**) solutions have been widely tested as a **profilactic** approach in specific populations, it has not proven useful[1,2,3,4].

❖In contrast, use of ELT for the **treatment** of C-RBSI is promising[5].

❖However, there are not enough data to recommend ELT as a therapeutic solution (C-III).

❖There is **no** clear **consensus** on the optimal regimen. In addition, **findings** on efficacy, concentration, use of anticoagulants, and adverse effects are controversial[6,7,8].


REVIEW

Pros and cons of catheter lock solutions

Vandana D. Nayyar[a] and Charmaine E. Lok[b]

Curr Opin Nephrol Hypertens 2013, 22:669–674

[1] Broom et al. BMC Nephrol 2012.

[2] Worth et al. J Hosp Infect 2014.

[3] Timsit et al. Am J Resp Crit Care Med 2015.

[4] Sofroniadou al. Hemodial Int 2017.

[5] Raad et al. Antimicrob Ag Chemother 2016.

[6] Hogan et al. Antimicrob Ag Chemother 2016.

[7] Raad et al. Antimicrob Ag Chemother 2013.

[8] Donlan et al. Clin Infect Dis 2011.

OBJECTIVE

To test different combinations of **ethanol lock solutions and heparin** in an **in vitro model** in order to find the most suitable ethanol lock therapy (**ELT**) regimen using the **minimum concentration** of the components to **eradicate biofilms** produced by various microorganisms.

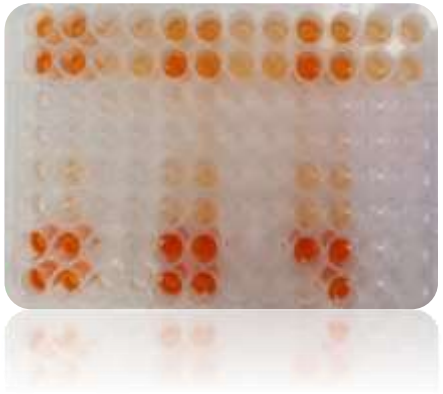
MATERIAL AND METHODS

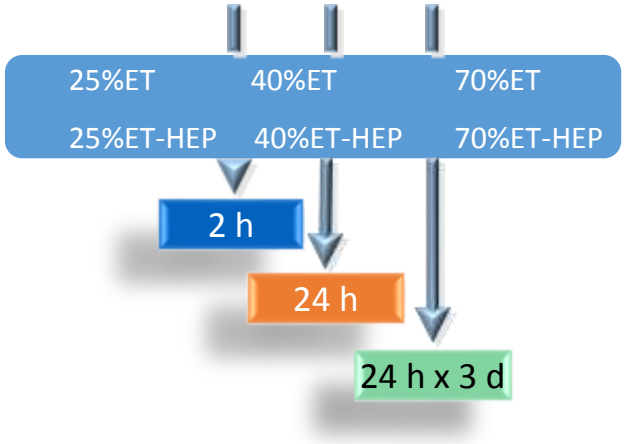
24-h biofilm

- *Staphylococcus aureus* ATCC25923
- *Staphylococcus epidermidis* (clinical strain)
- *Enterococcus faecalis* ATCC33186
- *Escherichia coli* ATCC25922
- *Candida albicans* ATCC14058

XTT assay

(absorbance at 490 nm in spectrophotometer)





270 experiments

Heparin activity

(Anti-Xa assay)

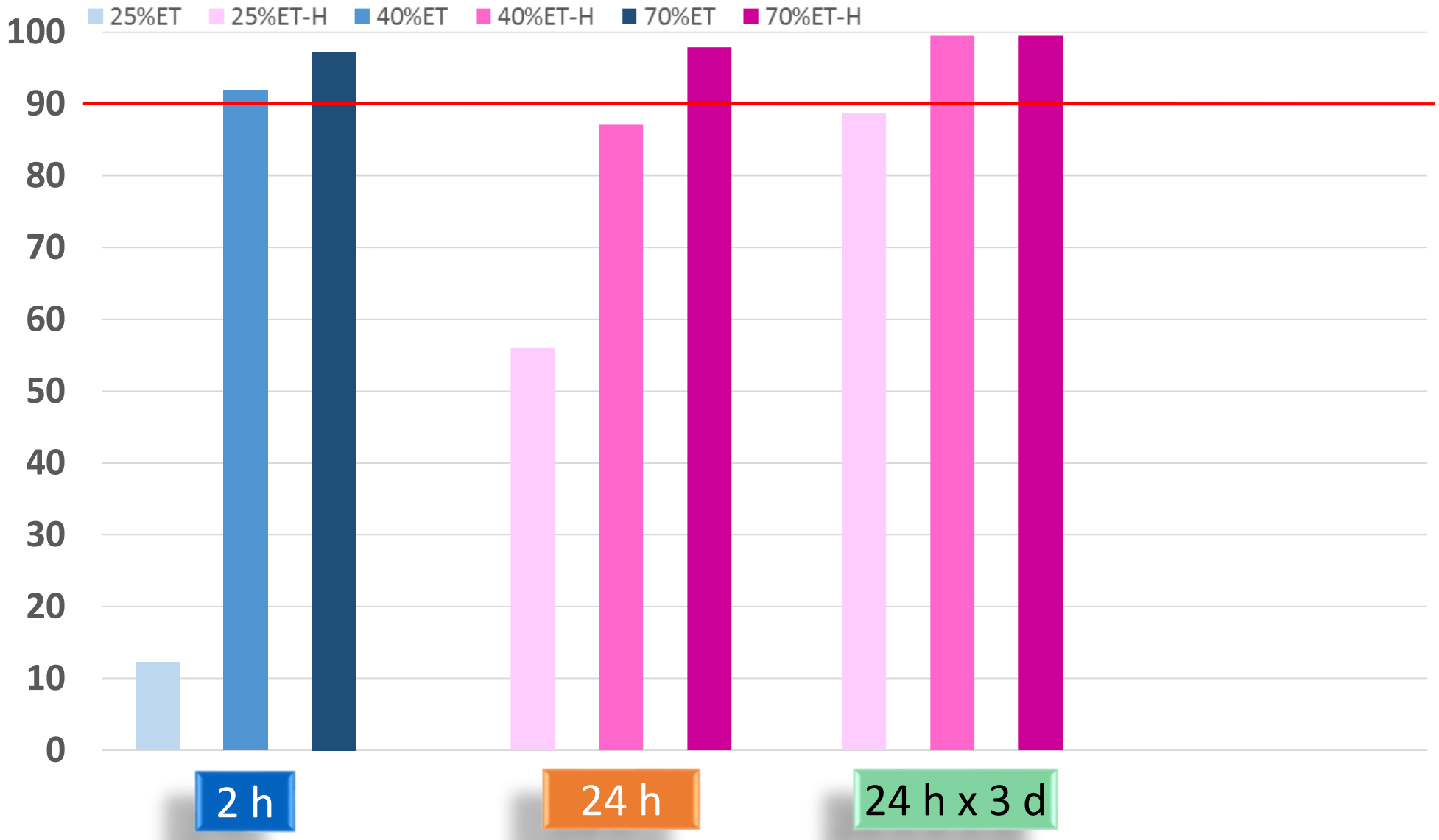
Reduction in metabolic activity (%)

Inhibition of re-growth at 24 h (%)*

* Only for the best regimen deteted

Efficacy was defined as **≥90%** reduction in metabolic activity or inhibition of re-growth

Median Reduction of metabolic activity (%)

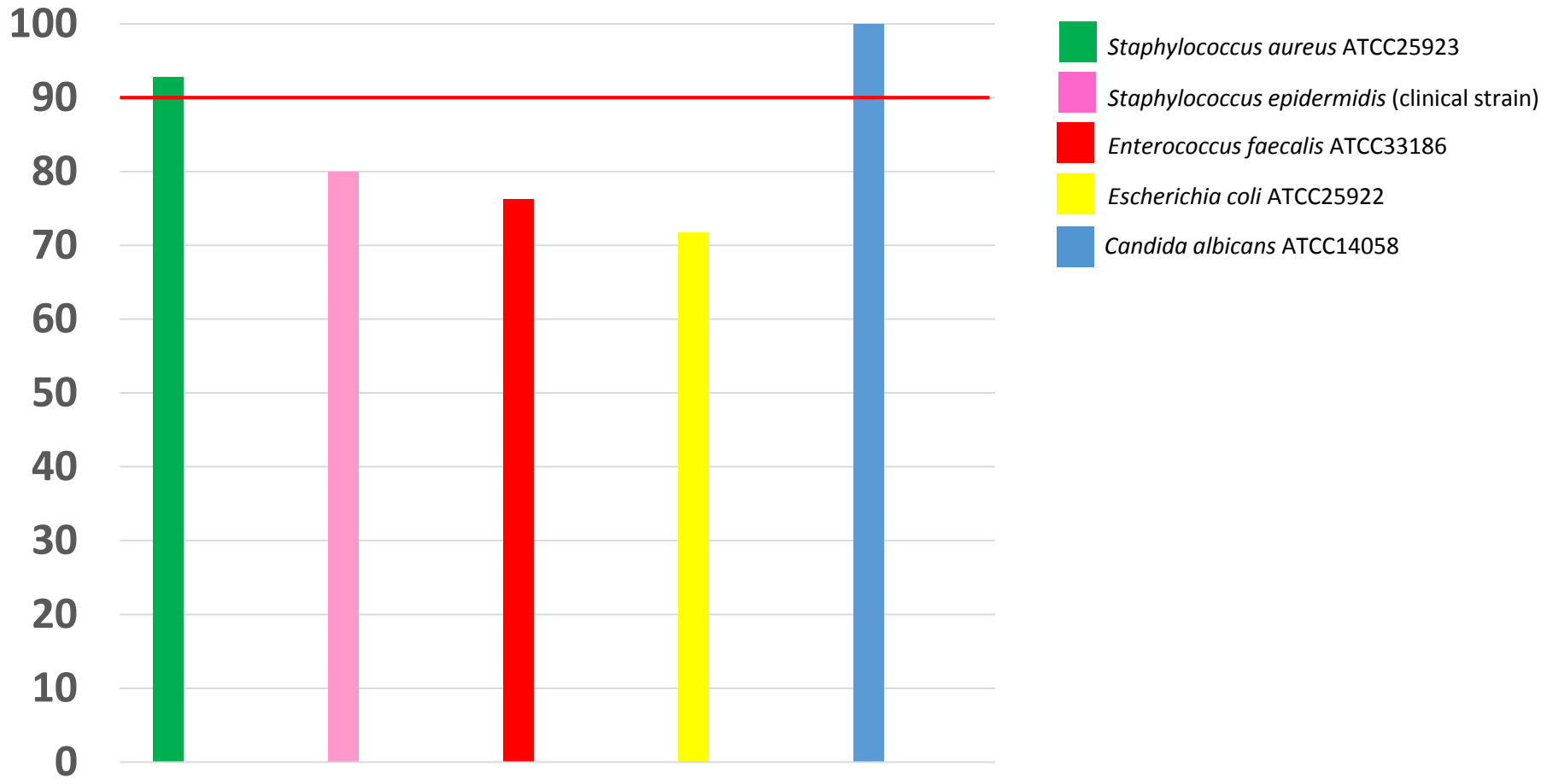


Median inhibition of re-growth at 24 h (%) by species

40%ET-HEP

3-day therapy

24 h



CONCLUSIONS

- ELT solutions: **40% ethanol** + 60 IU **heparin,** maintained ≥24 hours, **3-day course of therapy**
- Future studies: **optimize** and increase ethanol penetration and activity for complete eradication
- Assess evaluation of the efficacy of ELT in the **clinical setting**

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