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Risk and safety of Enterococci in probiotic use

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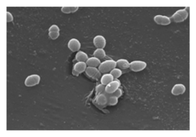
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The genus *Enterococcus*

Gram-positive cocci initially described as streptococci (untill 1980s)
Enterococcus = 3rd-largest genus of lactic acid bacteria (LAB)
after *Lactobacillus* and *Streptococcus*.



Most enterococcal species can grow in harsh conditions:
(6.5% NaCl, 40% bile salts, pH 9.6, T°: 10 to 45°C)

E. faecalis and *E. faecium* = most important species of *Enterococcus*

in medical and food microbiology and studied as potentiel probiotics.

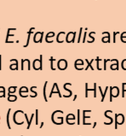
Habitat of *Enterococcus*

Enterococci occur in many different habitats :
Soil, surface water, sewage, plants, gastrointestinal tract of humans and animals
Presence in foods of animal origin (fermented and cooked meats, cheese).

E. faecalis = predominant *Enterococcus* species of the human gastrointestinal tract
In faeces : 10^5-10^7 CFU/g for *E. faecalis*
10^4-10^5 CFU/g for *E. faecium*



Enterocci are also present in the intestine of animals.
This leads to contamination of milk and meat.
They can survive pasteurization due to their heat resistance.



RISK

Pathogenicity of *Enterococcus*



Enterococcus belongs to LAB,
but there is controversy over considering them as GRAS
(Generally Recognized As safe)

In the last decades, they have emerged as important nosocomial pathogens causing a variety of infections in immunosuppressed and intensive care unit patients : endocarditis, bacteremia, infections of the urinary tract…

E. faecalis predominates among enterococci isolated from human infections (more than 80%).

Antibiotic resistance of *Enterococcus*

Resistance to a wide variety of antibiotics = contributing factor to pathogenesis

Intrinsic resistance : genes located on the chromosome
(β-lactams, cephalosporins, clindamycins, aminoglycosides)



Acquired resistance : genes on plasmids and transposons that can be transfer between strains.
(chloramphenicol, erythromycin, clindamycins, aminoglycosides, tetracycline, β-lactams, fluoroquinolones and glycopeptides such as vancomycine),

Vancomycin : antibiotic considered a last resort for treatment of multiple resistant enterococcal infections.
The emergence of vancomycin-resistant enterococci (VRE) in hospitals has led to infections that cannot be treated with conventional antibiotic therapy.

Virulence factors of *Enterococcus*

Virulence factors enhance the ability of a microorganism to cause disease.

Some virulence factors of *E. faecalis* are involved in :
- attachment to host cell and to extracellular matrix proteins (AS, Esp, EfaA..)
- resistance to macrophages (AS, HypR..),
- cell and tissue damage (Cyl, GelE, SprE..)
- immune system evasion (capsular polysaccharides).

Virulence factors are encoded by chromosomal regions
Or plasmid genes : transmissible to other strains by gene transfer.
E. faecium generally contains less virulence factors than *E. faecalis.*

SAFETY

Enterococcus in food technology

Use as dairy starter cultures,
Role in improving flavour and quality of cheese.
Contribution to the ripening and aroma
due to proteolytic and esterolytic activities
production of diacetyl and volatile compounds.



Production of bacteriocins, called enterocins
(for example Enterocin A, Enterocin B and Enterocin P).
Small peptides with antimicrobial activity
towards closely related Gram-positive bacteria
including spoilage or pathogenic bacteria, such as *Listeria.*



Use of bacteriocin-producing enterococci as starter cultures or protective cultures, or direct addition of the enterocins in food fermentation process may help to prevent the growth of pathogens.

Enterococcus as probiotics : some examples

E. faecium SF68 (NCIMB10415), (Cerbios Pharma)
found in Cylactin® and Bioflorin ®
Treatment of diarrheoea
It is considered as an alternative to antibiotic treatment.





Symbioflor® 1 (Symbiopharm)
contains *E. faecalis*
for recurrent infections of the upper/lower respiratory tracts,
inflammation of nasal sinuses (sinusitis) and bronchi (bronchitis).

SymbioPet : nutritional supplement for dogs and cats
contains *E. faecium*
stabilizes and reinforce the intestinal flora.

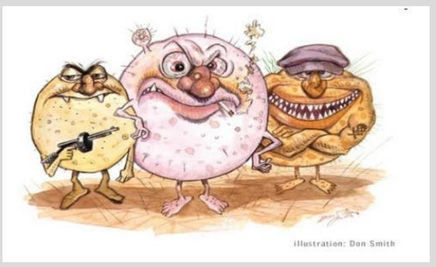




For safety assessment, antibiotic resistance and virulence factors must be checked in each new *Enterococcus* isolate before use as probiotic.

Regulatory situation in Europa

The EU approach related to, for example, *E. faecium* is focused on demonstrating that the strain is safe and that safe strains can be differentiated from those that cause nosocomial infections in hospitals and possess antimicrobial resistance (AMR) genes.
The EU Commission, EFSA and the EU food and feed industries recognize that *E. faecium*, other lactic acid bacteria and *Bacillus* spp. are present in fermented foods, food supplements and pharmaceutical preparations. In the feed industry, they can also be used as feed additives, including fermented feeds such as silages.
In June 2017, EFSA published a draft version of a new guidance on the characterization of microorganisms, which contains useful information on how EFSA will potentially assess the safety of *E. faecium* : antibiotic resistance, markers of virulence… whole genome analysis.
https://www.efsa.europa.eu/sites/default/files/engage/170615_0.pdf





https://pentec-consulting.eu/enterococcus-faecium-is-it-safe-views-from-taiwan-usa-and-eu/