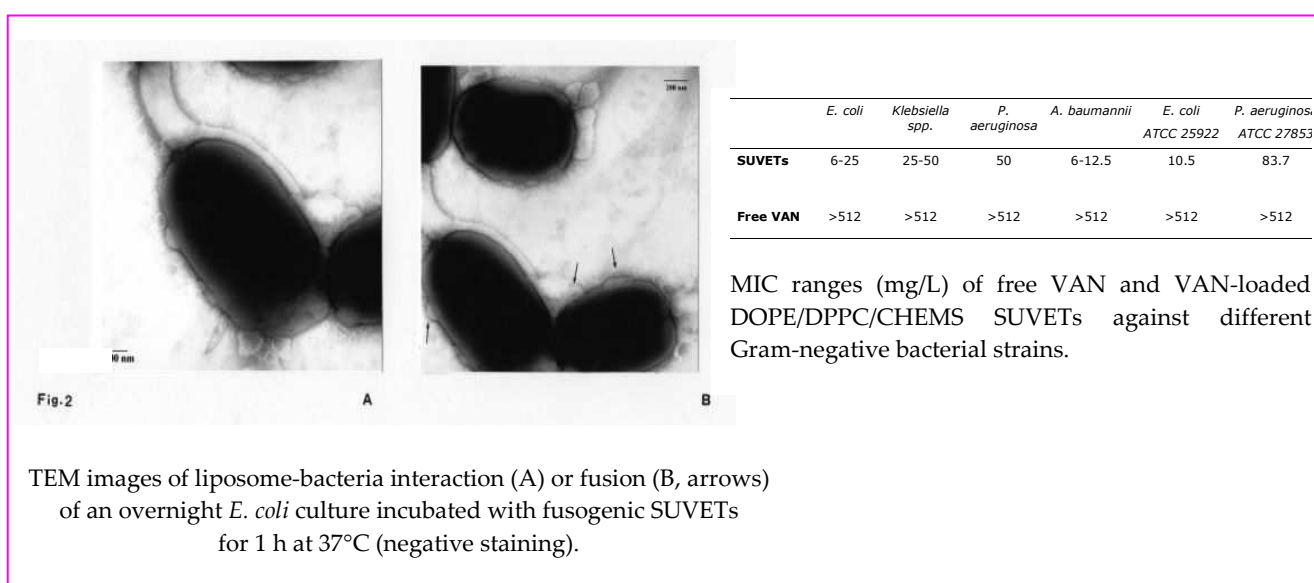


## Fusogenic liposomes for broadening the spectrum of action of antibiotics against gram-negative bacteria

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The University of Catania has developed a liposomal carrier systems based on a combination of fusogenic lipids. These liposomes, loaded with the glycopeptide antibiotics vancomycin and teicoplanin, showed to be able to inhibit *in vitro* the growth of wild and standard gram-negative bacterial strains.



TEM images of liposome-bacteria interaction (A) or fusion (B, arrows) of an overnight *E. coli* culture incubated with fusogenic SUVETs for 1 h at 37°C (negative staining).

### 1. Description of the product

Small unilamellar liposomes were prepared by the REV method, followed by using an extrusion procedure (SUVETs) from a phospholipid-cholesterol hemisuccinate mixture (DOPE:CHEM:DPPC, 4:4:2, mol/mol), known for its fusogenic properties with eukaryotic cell membrane. Glycopeptide antibiotics, such as vancomycin (VAN) and teicoplanin (TEP), were loaded with high efficiency in these vesicles. In the *in vitro* microbiological experiments, these systems showed to be able to inhibit to a different extent the growth of wild and standard gram-negative bacterial strains. For instance, MIC values as low as 6 mg/L were registered for VAN-loaded SUVETs against clinical isolates of *Escherichia coli* and *Acinetobacter baumannii*. In comparison, neither the free antibiotics nor drug-loaded 'classical' (non fusogenic) liposomes showed any activity against the same bacteria.

Scanning and transmission electron microscopy studies allowed to confirm that the produced SUVETs were able to adhere to and fuse with the external membrane of *E. coli*.

According to the preliminary experiments, this technological strategy can be proposed as a potentially successful way to enlarge the spectrum of activity of VAN.

### 2. Innovative aspect of the product

Many antibacterial agents, among which glycopeptides, are inactive against Gram-negative bacteria because of their incapacity to cross the outer membrane present in these bacterial cells. In this study we applied the strategy of fusogenic liposomes, up to now used to carry biological compounds and materials inside cells, to localize the antibiotics in the periplasmic space, thus allowing it to exert their bactericidal activity.

A specific potential application of this system can be for the treatment of severe burning and other skin lesions, where the proliferation of Gram negative bacteria is largely observed.

### **3. Main advantages of the offer**

- The proposed fusogenic liposomes are made with commercially available phospholipids (DPPC, DOPE) and a cholesterol derivative, that allow to obtain the formulation with a relatively low cost.
- Very high encapsulation efficiencies have been registered for both the tested drugs.
- Batch-to-batch reproducibility of SUVETS ( mean size, drug loading, etc.)
- Possibility of incorporating either hydrophilic (eg, salts) or lipophilic drugs, easily by varying the liposome production method.

### **4. Technology key words**

Antibacterial drug delivery; Liposomes; SUVET; DOPE; Gram- negative bacteria

### **5. Current Stage of Development**

Available for demonstration – field tested.

### **6. Intellectual Property Rights**

No IPR issue applied

### **Technical and scientific publications**

D. Nicolosi, M. Scalia, V.M. Nicolosi, R. Pignatello. Encapsulation in fusogenic liposomes broadens the spectrum of action of vancomycin against gram-negative bacteria.  
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