

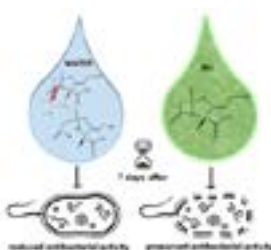
## A natural solvent improves $\beta$ -lactam antibiotic efficacy

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**Statement of the Problem:** World Health Organization declared bacterial infections by resistant pathogens a global crisis and place it among its priority lines of research. The aim of the present work is to improve the antibacterial efficacy of available molecules. We focus on beta-lactam antibiotics, a very useful therapeutic class of antibiotics, but unstable in the aqueous solvents of conventional formulations. That condition represents a clinical problem leading to therapeutic failure and antimicrobial resistance. We designed a new vehicle based on a natural deep eutectic solvent consisting on betaine and urea (BU). BU is capable of improving the stability of some beta-lactams including imipenem (IMP) the most unstable of the beta-lactam family. The main goal of the present work is to evaluate the therapeutic efficacy, the kinetics of IMP release, and the in vitro toxicological profile of the new solvent. Methodology: Killing curves of *Pseudomonas aeruginosa* incubated at 37°C, with IMP dissolved in BU in comparison with its aqueous solutions. Viability measures were made counting bacteria by flow cytometry using SytoBC<sup>®</sup>/ propidium iodide. The kinetic of IMP release was evaluated using a diffusional test based on a bicameral devise model. Data were analyzed applying Peppas Krosmyer equation. Cytotoxicity was evaluated using primary fibroblasts cultures. Findings: IMP-BU reduced the *P. aeruginosa* flow cytometry counting forty times compared to IMP aqueous solution (mean and SEM  $1,87 \times 10^7 \pm 3,91 \times 10^6$  and  $7,5 \times 10^8 \pm 3 \times 10^7$  respectively) in 24 hours. The value of the diffusional coefficient obtained ( $n=1,01$ ) indicates a case II release, consisting in a linear and progressive kinetics. Finally, the cytotoxicity assay of BU showed an IC<sub>50</sub> of 59,4 mg/ml, higher than the reported for others solvents of this class.

**Conclusion:** BU could represent a new biosafe natural alternative excipient to maintain IMP stability and therefore improve its efficacy.



## Biography

Belen Olivares has her expertise in stability and efficacy measurements of therapeutic molecules. Her study of a new solvent could create a new pathway applying no conventional solvents for improving clinical outcomes. She has built this idea after the experience in evaluation of the in-use stability of beta-lactams solutions for quality product evaluation.