Drug stability testing of continuous infusion of beta-lactam antibiotics for OPAT

GSASA research project

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Universitätsspital Basel

Project overview

Part 1


antibiotics MDPI

Article

Enhancing Stability and Investigating Target Attainment of Benzylpenicillin in Outpatient Parenteral Antimicrobial Therapy: Insights from In Vitro and In Vivo Evaluations

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Abstract: Background/Objective: Narrow-spectrum beta-lactam antibiotics such as benzylpenicillin and flucloxacillin are increasingly used in outpatient parenteral antimicrobial therapy (OPAT) programs to mitigate the adverse effects associated with broad-spectrum antibiotics. These beta-lactams require continuous administration via portable infusion devices during OPAT. However, the use of benzylpenicillin in OPAT requires special consideration because of its limited stability at elevated temperatures. **Methods:** We tested the benzylpenicillin stability, pH, and degradation of products in elastomeric pumps at different concentrations in saline and in buffered solution containing sodium citrate during a prolonged storage and at high temperatures (seven days at 2–8 °C followed by 24 h at 37 °C). Additionally, drug concentrations during intermittent bolus infusion and during OPAT were determined in five patients. The concentrations and degradation products of benzylpenicillin were measured using liquid chromatography mass spectrometry (LC-MS/MS). **Results:** Unbuffered benzylpenicillin solutions that were already degraded during refrigerator storage and analyte concentration were not measurable after 8 days. The stability of the buffered solutions was acceptable at all

check for updates

Citation: Rentsch, K.M.; Khanna, N.; Halbeisen, D.; Osthoff, M. Enhancing

Part 2

OPAT application

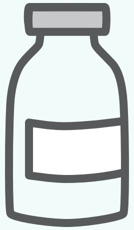
Zerbaxa®: ceftolozane/tazobactam

Zavicefta®: ceftazidime/avibactam

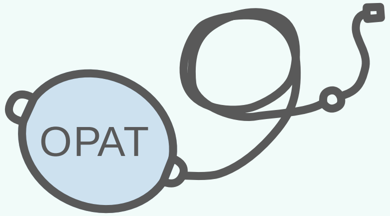
- Stability > 90 % ?
- Safety: pyridine

Methods

Preparation of 15 OPAT pumps (240 mL)

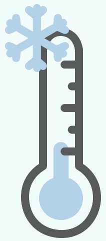


+ NaCl 0.9 %

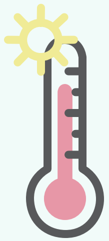


Zerbaxa®	Zavicefta®
3x 2.25 g	3x 3.75 g
3x 4.5 g	3x 7.5 g
3x 9.0 g	

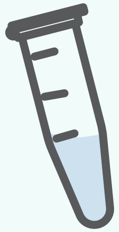
Incubation and sampling



2-8 °C
7 days
Sampling 2x



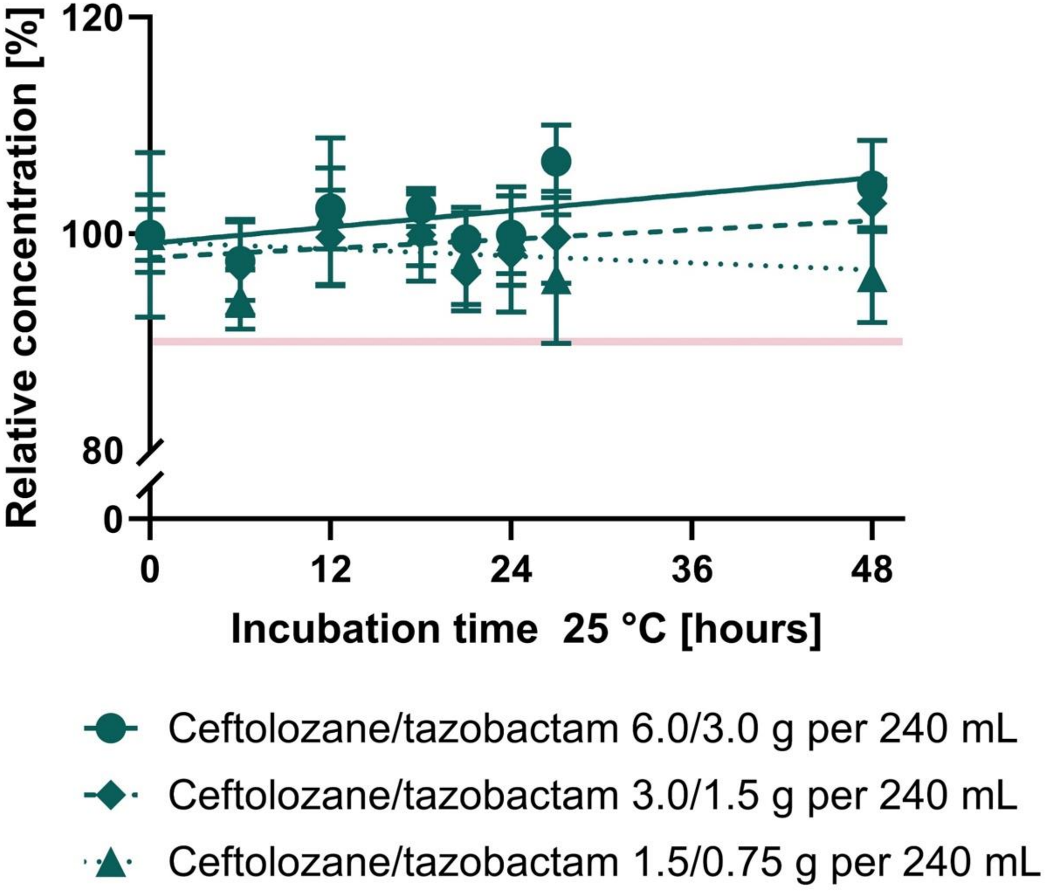
25 °C
48 hours
Sampling 7x



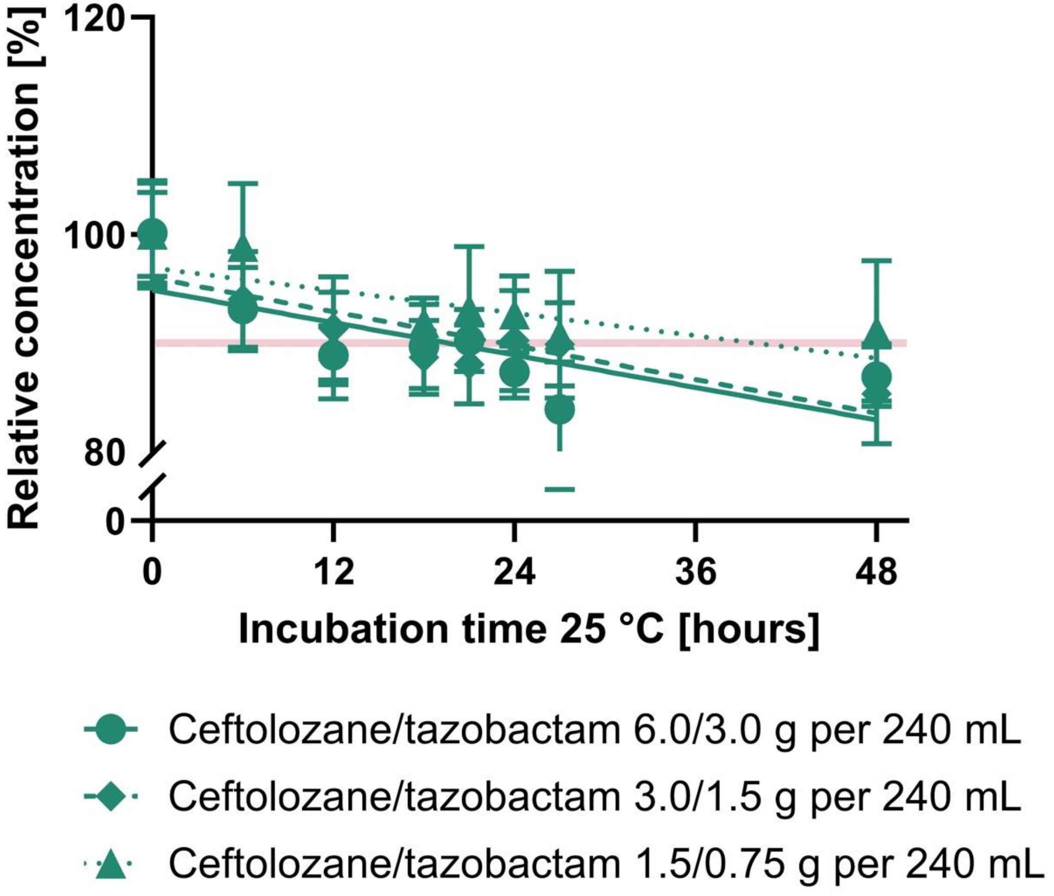
Quantification
Zerbaxa®
Zavicefta®, Pyridine

Stability of Zerbaxa® in OPAT

Ceftolozane

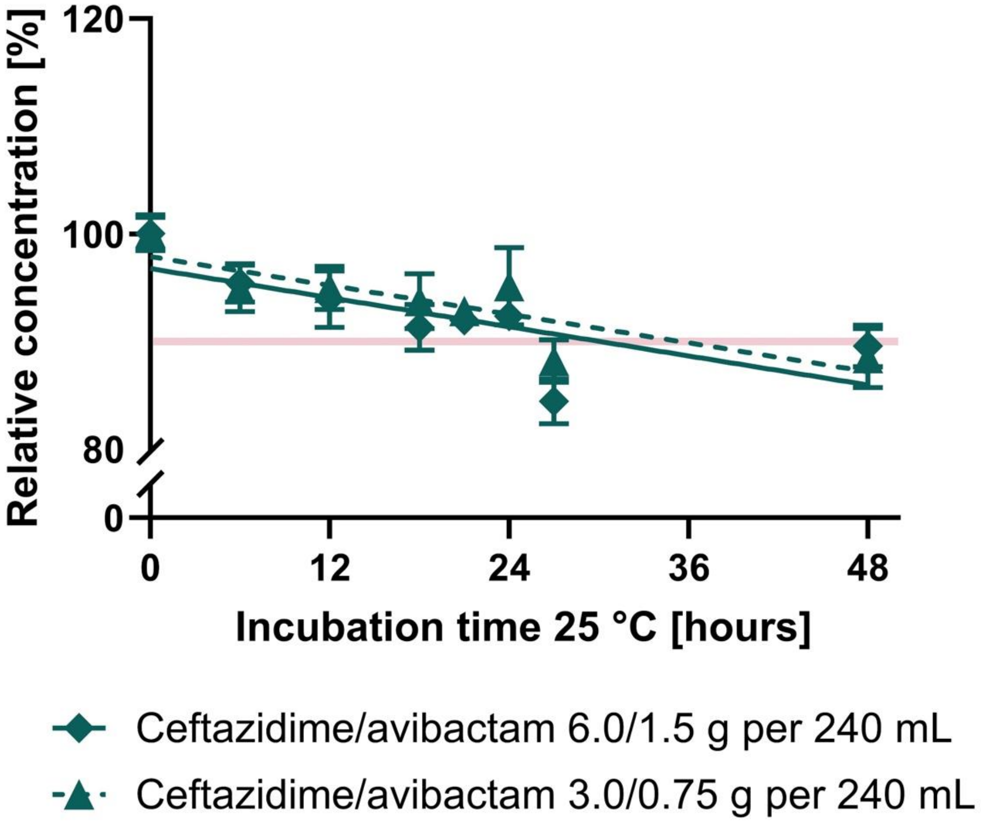


Tazobactam

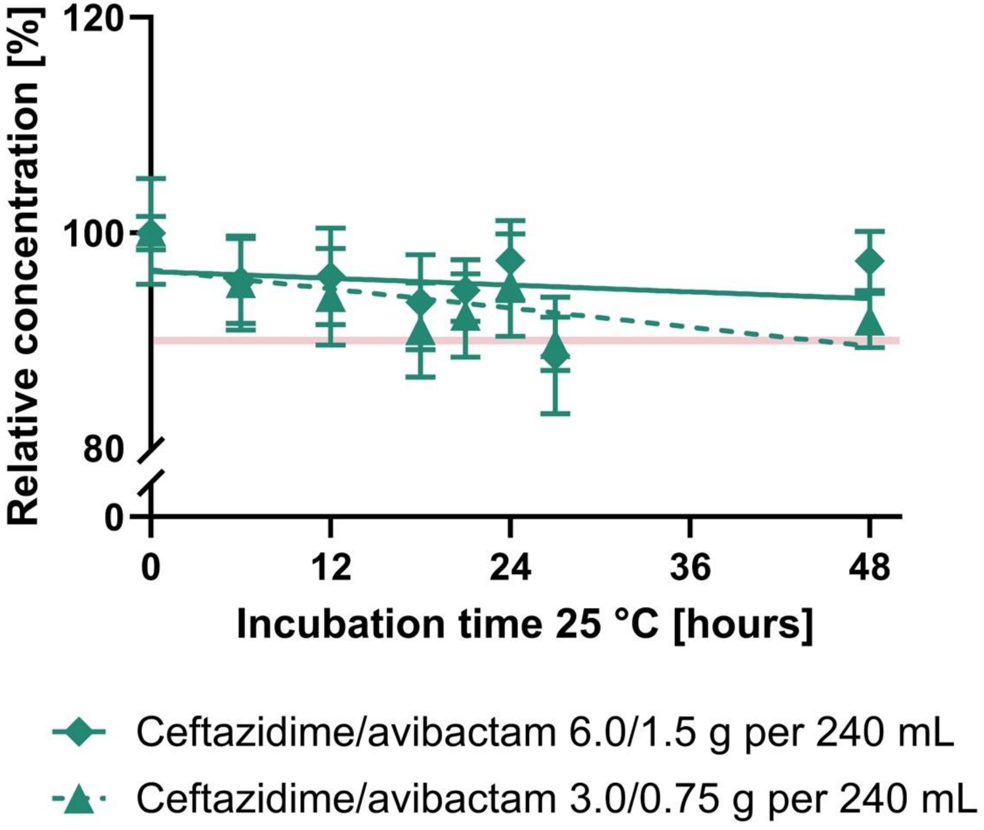


Stability of Zavicefta® in OPAT

Ceftazidime

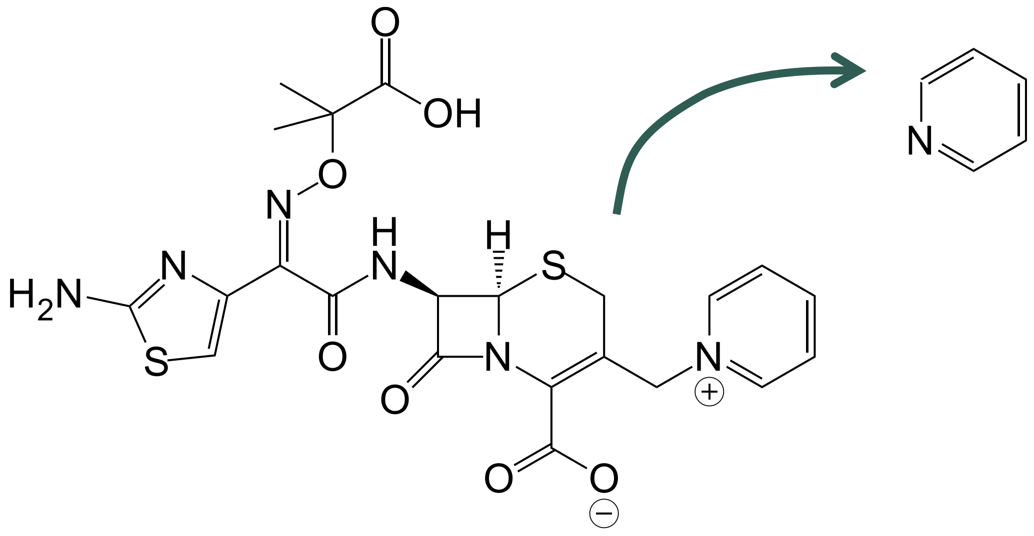


Avibactam



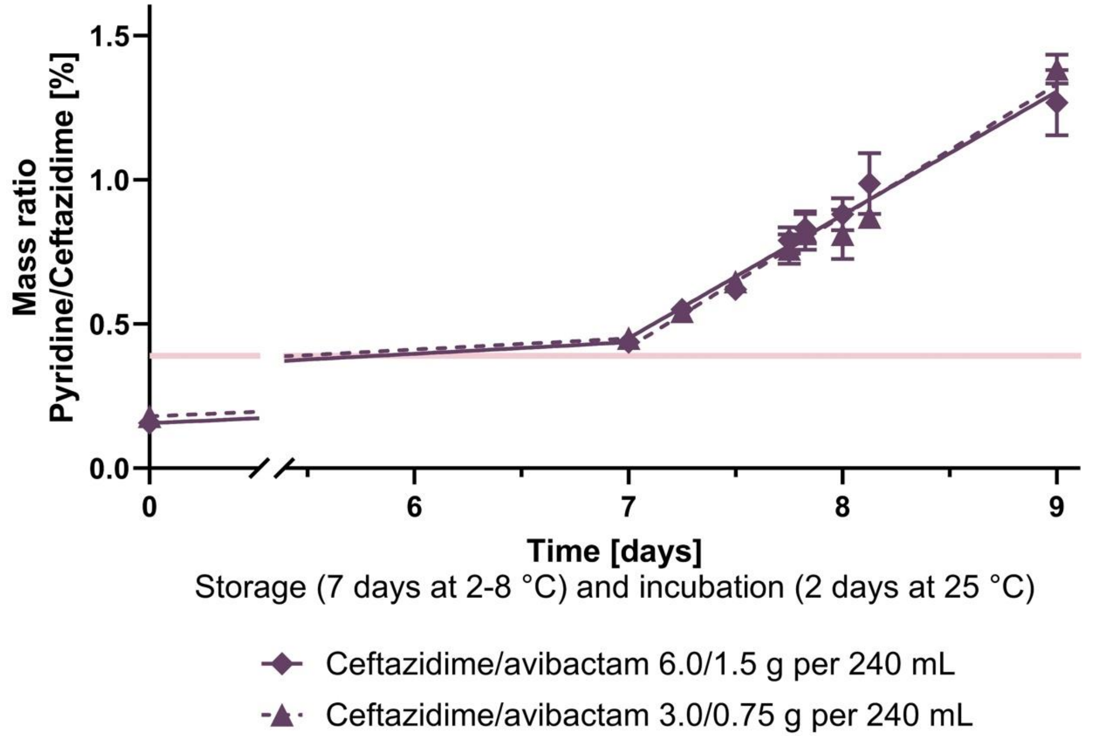
Safety of Zavicefta® in OPAT

Toxic degradation product



- Ph. Eur. Monograph 2344
- Impurity F: pyridine
- Limit: 0.4 % w/w pyridine/ceftazidime

Pyridine formation in elastomeric pumps

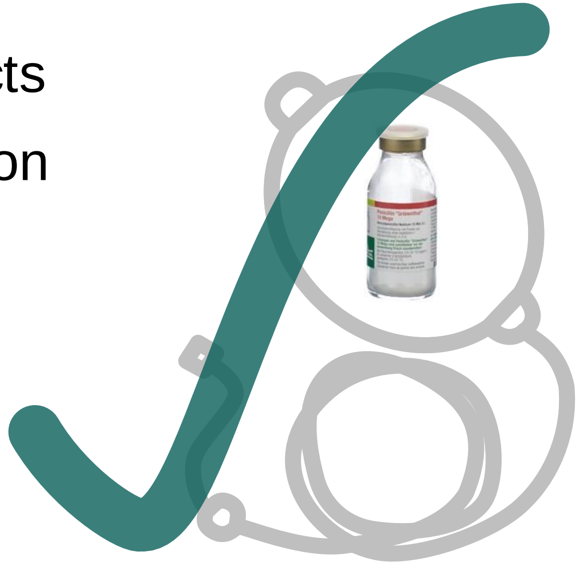


Summary

Part 1

Penicillin "Grünenthal"

- Flow rate
- Stability > 90%
- Degradation products
- Plasma concentration



Part 2

Zerbaxa®

Zavicefta®

- Stability < 90 %
- Pyridine limit

Thank you!

Schweizerischer Verein der Amts- und Spitalapotheker
Association suisse des pharmaciens de l'administration et des hôpitaux
Associazione svizzera dei farmacisti dell'amministrazione e degli ospedali
Swiss Association of Public Health Administration and Hospital Pharmacists

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- Julian Meier
- Delia Halbeisen
- Christoph Meier

- Sophia Rehm
- Joana Erdmann
- Katharina Rentsch

- Michael Osthoff
- Nina Khanna

References

Slide	Link
2	Pictures of vials: Pharmavista, HCI Solutions, Bern, Switzerland https://doi.org/10.3390/antibiotics13100970
6	Ph. Eur. 10.0, Monographie 2344
7	Pictures of vials: Pharmavista, HCI Solutions, Bern, Switzerland