

# Compatibility studies of seven commonly used drugs for parenteral administration in palliative care

Ursina Müller<sup>1,2</sup>, Fiona Haller<sup>3</sup>, Peter Wiedemeier<sup>1</sup>, Christian Steuer<sup>3</sup>

<sup>1</sup>Kantonsspital Baden AG; <sup>2</sup>Kantonsspitalapotheke Winterthur; <sup>3</sup>Institute of Pharmaceutical Sciences, Pharmaceutical Analytics, ETH Zurich

## 1 Introduction

Parenteral administration of drugs is often required in critical and palliative care because many patients cannot take drugs orally. Under these conditions continuous subcutaneous infusion (CSCI), containing e.g. morphine or levomepromazine, has become common practice [1]. However, there is limited data about the chemical compatibility over at least 24 h of the commonly used drug mixtures [2]. The objective of this study was to complete the binary compatibility recommendations in palliative care at Kantonsspital Baden AG (KSB) by analyzing compatibilities of fourteen binary and one ternary drug mixtures in order to increase patient safety and simplify ward handling.

## 2 Materials and Methods

Compatibility of fourteen binary mixtures and one ternary mixture (drug mixtures all stored at 4 °C and 25±3 °C) of the compounds in table 2 were tested by UHPLC in sodium chloride 0.9% and/or glucose 5% at 0 h, 4 h, 8 h, 24 h and 48 h at concentrations used clinically for CSCI. Drugs were purchased from several Swiss suppliers and from Runge Pharma Germany.

Table 1. UHPLC conditions

Apparatus	HITACHI ChromasterUltra UHPLC	t (min)	%ACN	%H <sub>2</sub> O	F (mL/min)
Column	ACE C18-AR, 100 x 2.1 mm, 1.7 µm	0	2	98	0.3
Detector	DAD	1	2	98	0.3
Temperature	40 °C	7.1	70	30	0.3
Injection volume	4 µl	7.3	100	0	0.5
		8.3	100	0	0.5
		8.5	2	98	0.3
		9.5	2	98	0.3

Table 2. Concentrations used for CSCI at KSB; Hal: Haloperidol lactate; Lev: Levomepromazine hydrochloride; Met: Metoclopramide hydrochloride; Sco: Scopolamine butylbromide; Mid: Midazolam hydrochloride; Mor: Morphine hydrochloride; Dex: Dexamethasone sodium phosphate. \* s.c.: off label use

API	Product	Dose / 24 h	Conc. in 20 mL
Sco	Buscopan 20 mg 1 mL	60 mg - 140 mg / 24 h	3 - 7 mg/mL
Lev	Levomepromazin neuraxpharm* 25 mg 1 mL	12.5 - 50 mg / 24 h	0.625 - 2.5 mg/mL
Dex	Mephameson* 4 mg 1 mL Mephameson* 8 mg 2 mL	4 - 8 mg / 24 h	0.2 - 0.4 mg/mL
Hal	Haldol* 5 mg 1 mL	5 - 10 mg / 24 h	0.25 - 0.5 mg/mL
Met	Primperan* 10 mg 2 mL	60 mg / 24 h	3 mg/mL
Mid	Dormicum* 5 mg 1 mL, Dormicum* 15 mg 3 mL Dormicum* 50 mg 10 mL	24 mg / 24 h	1.2 mg/mL
Mor	Morphin 10 mg 1 mL Morphin 100 mg 10 mL	40 - 100 mg / 24 h	2 - 5 mg/mL

## 3 Results and Discussion

Table 3. Compatibility recommendation at KSB. The recommendations are only valid for drug mixtures in sodium chloride 0.9% or glucose 5% at concentration ranges noted in table 2. LP: light protection

	Lev	Dex	Hal	Met	Mid	Mor
Sco	LP					
Lev		precipitation	LP	LP	LP	LP
Dex			precipitation	visual control	precipitation	visual control
Hal						
Met						
Mid						

Red: not recommended; green: compatible; orange: Dexamethasone: visual inspection of the mixture necessary.

## 5 References

- Bausewein C. et al., Besonderheiten der Pharmakotherapie in der Palliative Care. Bigorio, 2012
- Baker J et al., The current evidence base for the feasibility of 48-hour continuous subcutaneous infusions (CSCIs): A systematically-structured review, PLoS ONE 13(3): e0194236, 2018

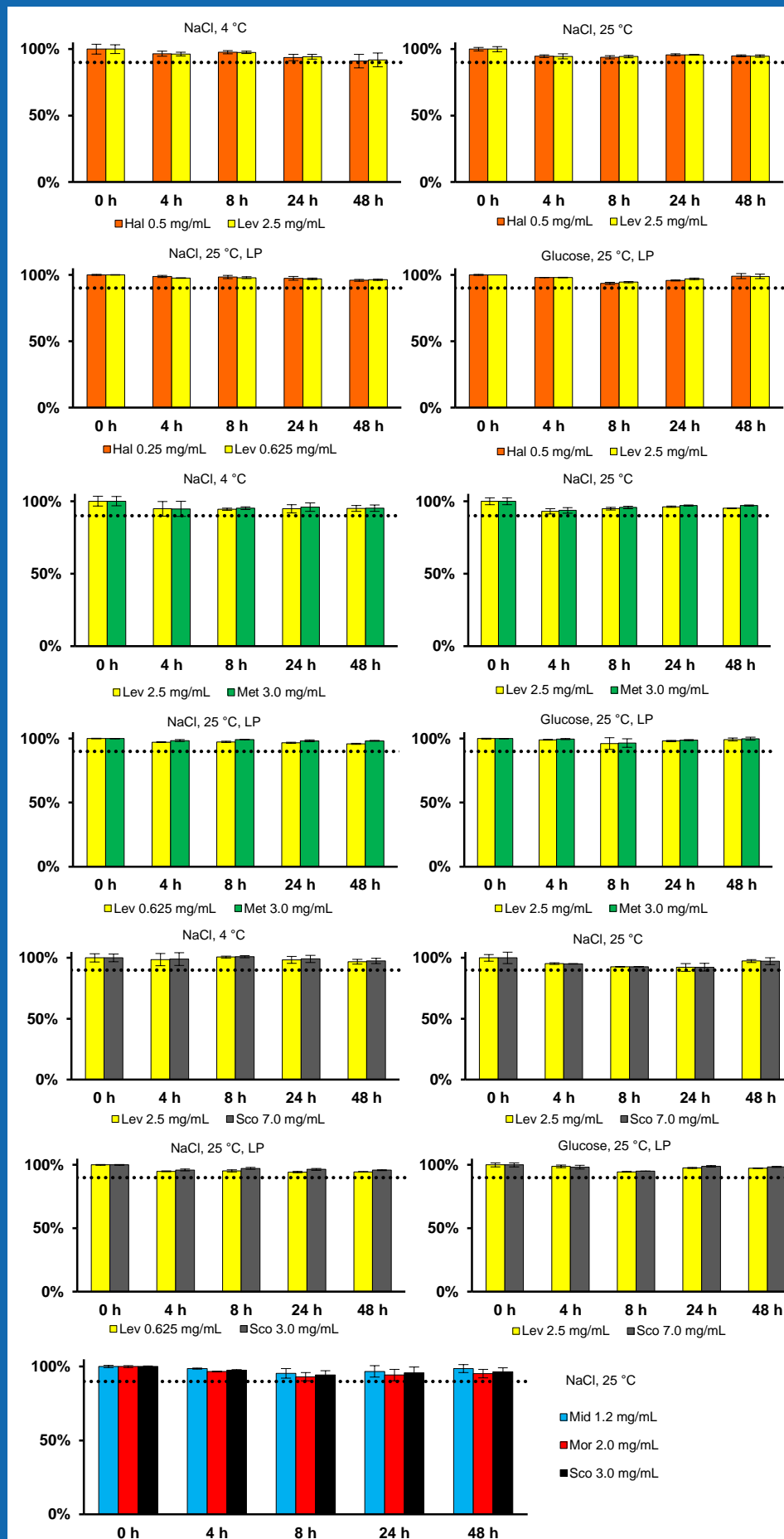


Figure 1. Results of the compatibility measurements of the drug mixtures. Measurements at 0 h were defined as 100%.

## 4 Conclusion

Compatibility recommendations for drug mixtures in palliative care at KSB could be completed with new data of combined mixtures in sodium chloride 0.9% and glucose 5%. In addition, the developed and validated method can be applied to generate more data on any required combination of the seven tested drugs.

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