

Background and Importance

Patients hospitalized in Intensive Care Units (ICUs) often require many drug infusions. Due to limited intravenous (IV) accesses, concomitant administration of drugs in the same infusion line is often necessary. Compatibility studies of Y-site administrations are already available in literature, but many data are lacking. Previous work (d'Huart *et al. Pharm Technol Hosp Pharm* 2019 ; 4,1 :29-40) identified a list of Y-site administration without compatibility data.

Aim and Objectives

To evaluate the physical compatibility of Nefopam with other drugs commonly used in ICUs, to secure their IV administration.

Material and Methods

For each mixture of Nefopam / drug B

80-160µg-2.5mg/mL



9/1
1/1
1/9



T 0H
T 1H
T 4H

Visual evaluation :

- Precipitation
- Colour change
- Gas formation

Subvisual evaluation :

- UV spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m²)
→ Evaluation of turbidity

- Particle counter (PAMAS SSVS) : Light Obscuration Particle Count Test

- Based on the principle of light blockage
- Automatic determination of the number of particles according to size
- Requirements for ≥ 10 µm and ≥ 25 µm particles

pH measurement
(Bioblock Scientific pH meter)



•Nefopam-Cefotaxime – T 0H
No visible particle at all ratios



20 pairs of mixtures :
Nefopam + 9 other drugs
Diluted in different solvents



Storage : 20-25°C

Visual evaluation :

No change from T 0H to T 4H
for each pair tested

Subvisual evaluation :

- UV spectrophotometry :
Absorbance values are stable
from T 0H to T 4H

- Particle counter :

≤ 6000 particles ≥ 10 µm
≤ 600 particles ≥ 25 µm
per container ≤ 100mL
according to European Pharmacopoeia (EP)
Reference Standards

→ **19 compatible pairs at all ratios**

→ **1 incompatible pair :**
Nefopam – Cefotaxime,
Particle counting at the 1/9 ratio
≥ 6000 particles ≥ 10 µm
at each time of analysis

pH measurement :
No change of more than 0.5 pH unit
for all mixtures from T 0H to T 4H

-Conc.: concentration
-D5W: 5% Dextrose
-D10W: 10% Dextrose
-NS : 0.9% Sodium chloride
-Isofundine®:
Sodium chloride, Potassium chloride,
Magnesium chloride, Calcium chloride

Results

Mixtures with Nefopam

DRUGS	CONC.	SOLVENT	RESULTS
Nefopam	160 µg/mL	Isofundine®	C
Nicardipine hydrochloride	1 mg/mL	None	C
Nefopam	160 µg/mL	NS	C
Nicardipine hydrochloride	1 mg/mL	None	C
Nefopam	160 µg/mL	Isofundine®	C
Pyridoxine hydrochloride	0.5 mg/mL	Isofundine®	C
Nefopam	160 µg/mL	NS	C
Pyridoxine hydrochloride	0.5 mg/mL	Isofundine®	C
Nefopam	160 µg/mL	NS	C
Pyridoxine hydrochloride	0.5 mg/mL	NS	C
Nefopam	160 µg/mL	Isofundine®	C
Thiamine hydrochloride	0.5 mg/mL	Isofundine®	C
Nefopam	160 µg/mL	NS	C
Thiamine hydrochloride	0.5 mg/mL	Isofundine®	C
Nefopam	160 µg/mL	NS	C
Thiamine hydrochloride	0.5 mg/mL	NS	C
Nefopam	160 µg/mL	NS	C
Tramadol hydrochloride	6.3 mg/mL	NS	C
Nefopam	160 µg/mL	NS	I
Cefotaxime sodium	40 mg/mL	D5W	I
Nefopam	80 µg/mL	Isofundine®	C
Calcium chloride	2 mg/mL	Isofundine®	C
Nefopam	80 µg/mL	NS	C
Calcium chloride	2 mg/mL	Isofundine®	C
Nefopam	80 µg/mL	NS	C
Calcium chloride	2 mg/mL	NS	C
Nefopam	160 µg/mL	Isofundine®	C
Hydrocortisone sodium succinate	2 mg/mL	NS	C
Nefopam	160 µg/mL	NS	C
Hydrocortisone sodium succinate	2 mg/mL	NS	C
Nefopam	2.5 mg/mL	NS	C
Isosorbide dinitrate	1 mg/mL	None	C
Nefopam	160 µg/mL	Isofundine®	C
Magnesium sulfate	3 mg/mL	D10W	C
Nefopam	160 µg/mL	NS	C
Magnesium sulfate	3 mg/mL	D10W	C
Nefopam	160 µg/mL	Isofundine®	C
Magnesium sulfate	4.5 mg/mL	D10W	C
Nefopam	160 µg/mL	Isofundine®	C
Magnesium sulfate	4.5 mg/mL	NS	C

C : compatible and stable for 4 hours **I** : incompatible

Conclusion and Relevance



19/20 mixtures with Nefopam were compatible and stable for 4 hours.
It brings new compatibility data to the literature.



The Nefopam (160 µg/mL – NS) – Cefotaxime (40 mg/mL – D5W) pair was incompatible.

The physical compatibility of drugs does not allow to conclude to the chemical stability.

These results are valid in pairs and cannot be extrapolated for mixtures of more than 2 drugs.