COMPATIBILITY AND STABILITY OF ONDANSETRON AND MIDAZOLAM MIXTURES USED IN PALLIATIVE CARE

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BACKGROUND AND IMPORTANCE

There are different factors that can influence the compatibility and stability of the mixture: drug type, concentration, solvent, container, temperature and light. There are some mixtures of drugs with proven stability, but there is lack of evidence about the stability and compatibility of the combination of ondansetron and midazolam. The objective of this investigation is to study the compatibility and stability of a binary mixture of these drugs in solution for subcutaneous infusion in palliative care

AIM AND OBJECTIVES

To evaluate the compatibility and stability of two admixtures of ondansetron and midazolam at two different temperatures (25ºC and 37ºC). The concentrations of the admixtures are: 0.1 g/L - 0.1 g/L; 0.5 g/L - 1.0 g/L in NaCl 0.9% stored in elastomeric infusors protected from light.

MATERIAL AND METHODS

Concentration of each drug was periodically determined by using a HPLC-UV and UV-Vis spectrophotometry methods into analytical chemistry laboratory between February and June of 2019. Standard solutions were prepared by adequate dilution from the sample. The standard were divided into different aliquots parts, stored in Eppendorf tubes and frozen until each day of analysis

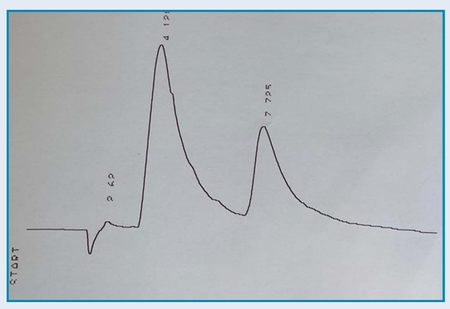
HPLC-UV

- Shimadzu LC-6A pump equipped with Rheodine 7125 injection valve 20 µL, a Shimadzu SPD-6A spectrophotometric detector
- Column: LiChrospher ® 100 C18 (5 µm) LiChroCART® 250-4 column
- Mobile phase: methanol:KH_2PO_4 0.05 M, adjusted to pH 3 with H_3PO_3 (60:40, v/v)
- Flow rate: 1.0 mL/min
- λ=254 nm
- Retention time (Ondansetron): 4.1 min ; Retention time (Midazolam): 7.8 min

UV-spectrophotometry

- λ=250 nm; λ=310 nm
- A(250 nm) = 0.0534[ondansetron] + 0.0444[midazolam] +0.2590
- A(310 nm) = 0.0490[ondansetron] + 0.0017[midazolam] + 0.2096

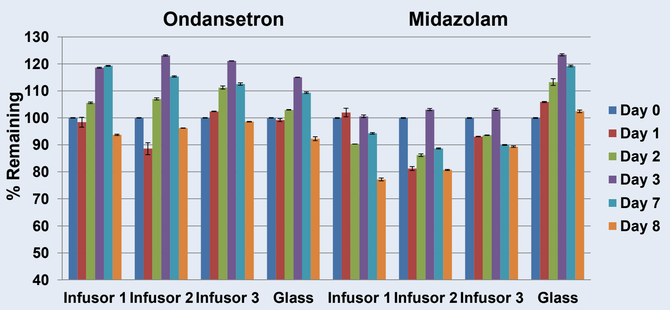
RESULTS



HPLC-UV and UV-Vis spectrophotometric methods gave the same results respect to stability of the mixtures diluted in NaCl 0.9%:
ondansetron-midazolam (0.1 mg/mL-0.1 mg/mL and 0.5 mg/mL-1.0 mg/mL) are stable (retained >90% of their initial concentrations) only one day at 25ºC and 37ºC respectively as can be see in the subsequent graphics

HPLC-UV

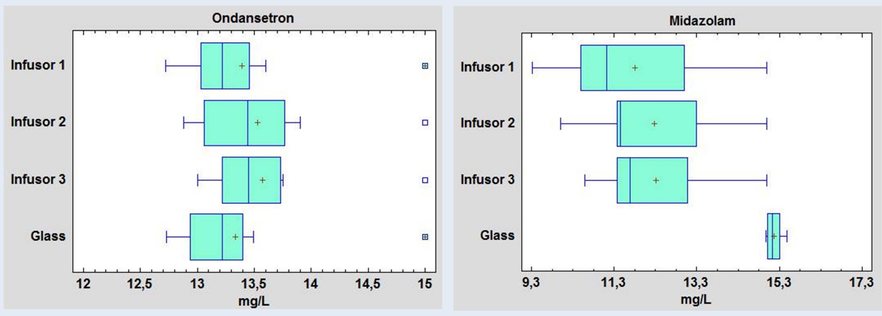
0.1 mg/mL – 0.1 mg/mL 25ºC
Ondansetron – Midazolam



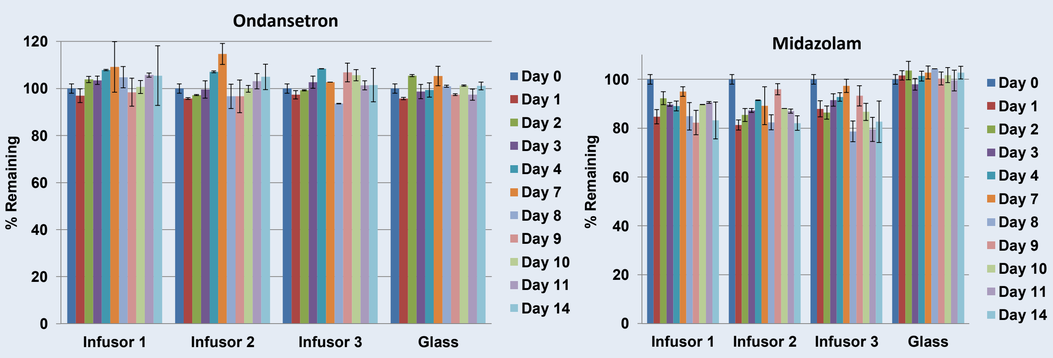
Standard solutions
Ondansetron – Midazolam
mg/L – mg/L
5.0 – 5.0
10.0 – 10.0
15.0 – 15.0
20.0 – 20.0
25.0 – 25.0

UV-SPECTROPHOTOMETRY

0.1 mg/mL – 0.1 mg/mL 25ºC
Ondansetron – Midazolam

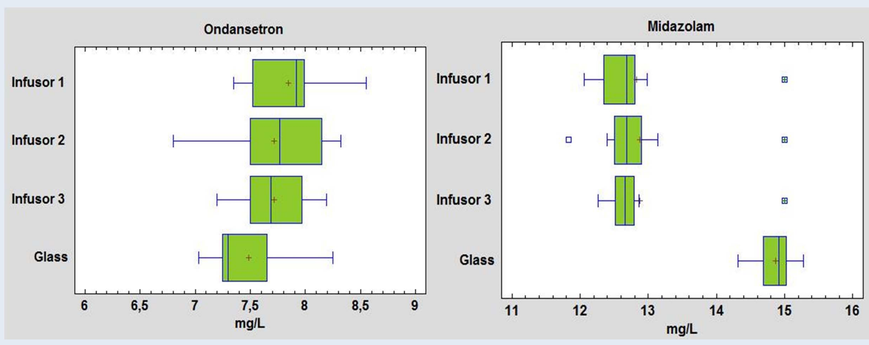


0.5 mg/mL – 1.0 mg/mL 37ºC
Ondansetron – Midazolam



Standard solutions
Ondansetron - Midazolam
mg/L – mg/L
2.5 – 5.0
5.0 – 10.0
7.5 – 15.0
10.0 – 20.0
12.5 – 25.0

0.5 mg/mL – 1.0 mg/mL 37ºC
Ondansetron – Midazolam



CONCLUSION AND RELEVANCE

It is recommended to use for a maximum of one day, at the concentrations evaluated, over time it tends to precipitate. Infuser conditioning decreases stability with respect to other conditioning materials, so other stability studies may not be extrapolated if stored under different conditions.

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