3PC-016

STABILITY EVALUATION OF FOUR METHADONE INTRAVENOUS MIXTURES USED IN PALLIATIVE SEDATION

Martín Bartolomé M[1,3], García Moreno FJ [1,3], Moral Carretón M [2,3], Sánchez Isac M [2,3], Borhidan RM[3], Villanueva Bueno C [1,3], Del Barrio Buesa S [1,3], Carrillo Burdallo A [1,3], Prieto Romero A [1,3], Herranz Alonso A [1,3], Sanjurjo Sáez M[1,3].

[1] Pharmacy Department. Hospital General Universitario Gregorio Marañón Madrid, Spain. [2] Palliative Care Unit. Hospital General Universitario Gregorio Marañón, Madrid, Spain. [3] Gregorio Marañón Institute of Health Research, Madrid, Spain.

BACKGROUND AND IMPORTANCE

In palliative care, drug infusions containing opioids are commonly used, but stability data regarding methadone mixtures is limited.

AIM AND OBJECTIVE

To evaluate the physicochemical stability of four quaternary mixtures containing methadone in different diluents and storage conditions, as well as to validate a HPLC method for this purpose.

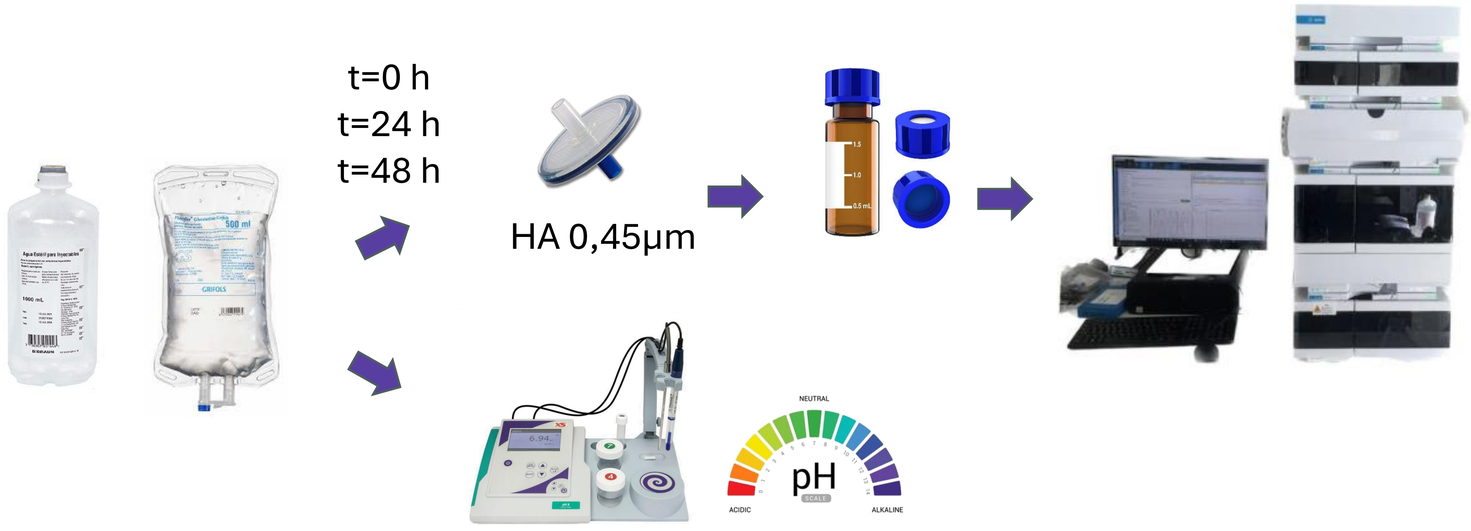
MATERIALS AND METHODS

Figure 1: *Studied mixtures agreed with palliative care physicians.*

Methadone 5mg Midazolam 30mg Butylscopolamine 60mg Haloperidol 5mg	Methadone 250mg Midazolam 250mg Butylscopolamine 240mg Haloperidol 30mg
M1: Saline 0,9% 250mL **M2**: Glucosaline 1/3 500mL	**M3**: Saline 0,9% 250mL **M4**: Glucosaline 1/3 500mL

Figure 2: *Chromatographic conditions for RP-HPLC-DAD.*

Stationary phase	*Kinetex* © C18, 100 x 4.6 mm, 2.6 µm	**Flow rate**	0.6 mL/min
Mobile phase	Monopotassium phosphate buffer 10 mM in H_2O (pH= 2.5): methanol	**Injection volume**	1 µL
Gradient	0-10min 75:25; 11-18min 60:40; 19-23min 75:25	**Column T[a]**	25ºC
		Detector wavelength	220 nm



Physicochemical stability was defined as:

- Absence of visual changes.
- Not significat pH variation.
- Remaining [drug] 90-110% of initial one (t_0).

RESULTS

A linear regression equation was obtained for each drug studied to validate the method. The coefficient of determination showed the method was linear in the range of concentrations considered.

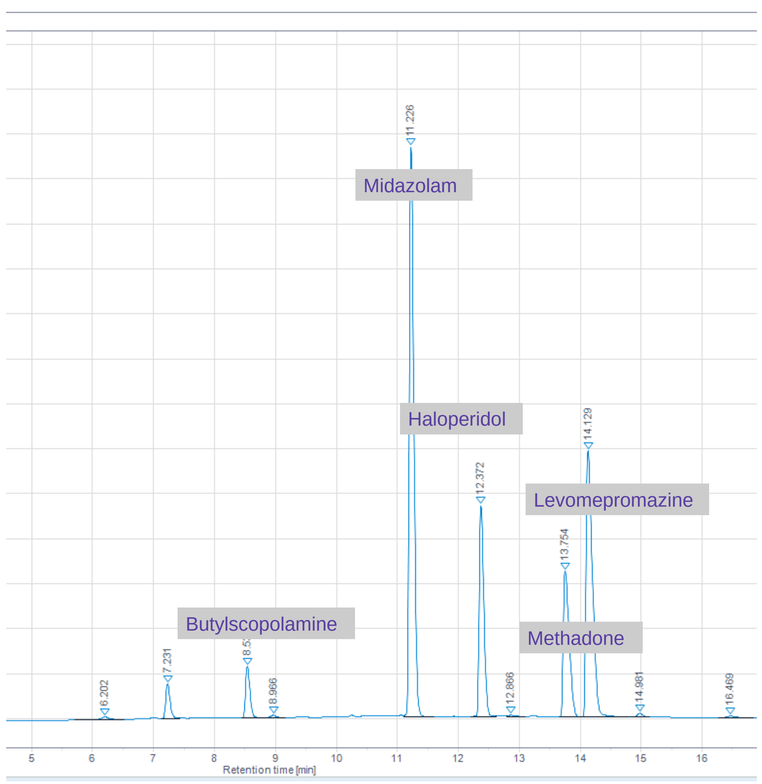
Time of retention for each drug, in minutes, was as follows:

-Butylscopolamine: 8.54 -Haloperidol: 12.37

-Midazolam: 11.23 -Methadone: 13.76

Precision and accuracy were also evaluated. Selectivity and specificity were confirmed by 2D-UV spectral analysis.

After 24 and 48 hours all mixtures met the predefined stability criteria, staying the drug concentrations at 90-110% of the initial one (t_0).



CONCLUSION AND RELEVANCE

The HPLC method was successfully validated. All four methadone mixtures remained stable for 48 hours under both light-exposed and ligth-protected conditions. This confirms their stability and suitability for use over this period.

mmbartolome@salud.madrid.org @farma_gregorio www.madrid.org/hospitalgregoriomaranon/farmacia