STABILITY OF MIXTURES OF ONDANSETRON AND HALOPERIDOL STORED IN INFUSORS AT DIFFERENT TEMPERATURES

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BACKGROUND

Mixing different drugs for use in continuous infusion systems is a common practice in palliative care, but the analytical study of compatibility and stability is not always available.

PURPOSE

To evaluate the compatibility and stability of two admixtures of ondansetron and haloperidol at two different temperatures (25ºC and 37ºC). The concentrations of the admixtures are: 0.15 mg/mL–0.25 mg/mL and 0.3 mg/mL–0.4 mg/mL of haloperidol and ondansetron respectively in NaCl 0.9% stored in elastomeric infusors protected from light.

MATERIAL AND METHODS

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): 3.6 min ; Retention time (Haloperidol): 6.6 min

REGRESSION EQUATIONS FOR ADMIXTURES

Admixtures Haloperidol-Ondansetron	T ºC	Drug	Regression equation
0.150 – 0.250 (mg/mL) *Standard solution*[b] Haloperidol (3, 6, 7.5, 9) mg/L Ondansetron (5, 10, 12.5, 15) mg/L	25ºC	Haloperidol	Slope: 15717.4 ± 871.1[a] Intercept: -13829.8 ± 5291.5[a] R^2 = 0.991
		Ondansetron	Slope: 23688.2 ± 2983.7[a] Intercept: -84090.8 ± 33566.6[a] R^2 = 0.970
	37ºC	Haloperidol	Slope: 15726.0 ± 1295.5[a] Intercept: -15264.1 ± 8744.9[a] R^2 = 0.987
		Ondansetron	Slope: 21284.1 ± 1766.1[a] Intercept: -59512.8 ± 19868.1[a] R^2 = 0.986
0.300 – 0.400 (mg/mL) *Standard solution*[b] Haloperidol (3, 6, 9, 12, 15) mg/L Ondansetron (4, 8, 12, 16, 20) mg/L	25ºC	Haloperidol	Slope: 14018.6 ± 803.9[a] Intercept: -15524.5 ± 7999.5[a] R^2 = 0.990
		Ondansetron	Slope: 20243.6 ± 1648.3[a] Intercept: -66565.0 ± 21867.6[a] R^2 = 0.980
	37ºC	Haloperidol	Slope: 13778.8 ± 494.0[a] Intercept: -9229.8 ± 4915.2[a] R^2 = 0.996
		Ondansetron	Slope: 19288.6 ± 960.8[a] Intercept: -45093.9 ± 12746.5[a] R^2 = 0.993

[a] Standard error for regression equation obtained by Statgraphics program

[b] 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

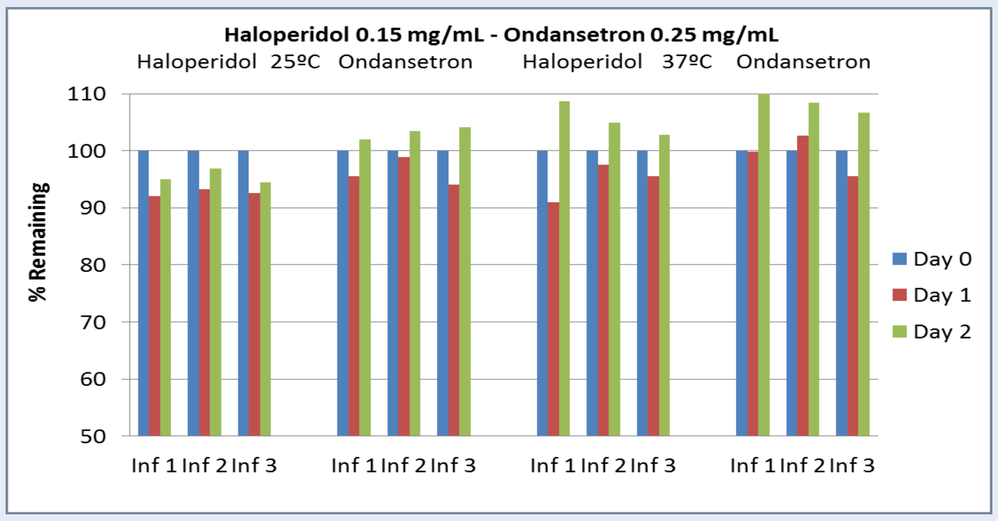
PHYSICAL STABILITY

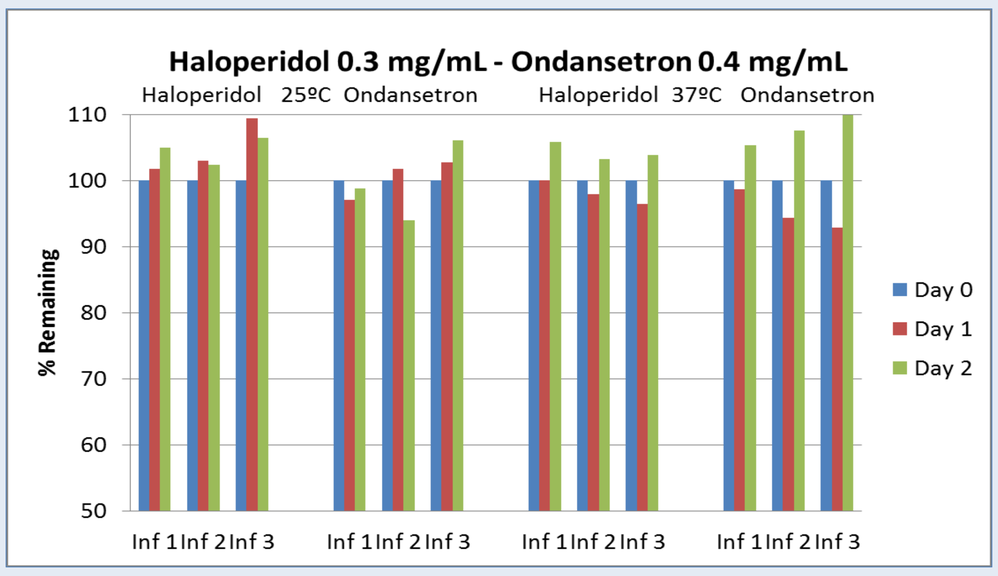
All solutions were initially clear and colourless but visible particles appear, in all cases, into the infusers after two days since their preparation.

CHEMICAL STABILITY

Admixtures diluted in NaCl 0.9% are as follow: Haloperidol-ondansetron (0.15 mg/mL – 0.25 mg/mL) is stable (retained >90% of their initial concentration) two days at 25ºC and 37ºC; (0.3 mg/mL – 0.4 mg/mL) is stable two days at 25ºC and 37ºC.

PERCENTAGES REMAINING





CONCLUSIONS

The mixture of haloperidol and ondansetron stored in infusor devices is not stable because visible particles appear in less than 48 hours. Physical pressure by the elastomeric infusor may have a role in the instability, since precipitate is not appreciated when stored in flask.