Introduction

Warfarin, a commonly used anticoagulant, is often administered to patients through feeding tubes. The administration of warfarin is complicated since dosages widely fluctuate from patient to patient due to a variety of factors [1-5]. Previous studies have suggested that warfarin administered through feeding tubes binds to nutrition, altering its bioavailability and reducing its therapeutic effect. Many hospitals have introduced new protocols to prevent this interaction. Nevertheless, a recent study proposed that warfarin, in addition to binding to nutrition injections, is adsorbing to patients’ feeding tubes in acidic environments [6].

In this study, we verify the interaction, provide evidence that contradicts the theory that this reaction is pH dependent, model the interaction using fluorescein and calculate a lower limit estimate of the equilibrium constant (K).

Materials and methods

Using ultraviolet-visible (uv-vis) spectrometry, we measured the absorbance of warfarin and fluorescein solutions before and after exposure to 75 centimeters of FLORIDA Dual Port Feeding Tube. Molar extinction coefficients from the standard absorbance curve (Fig.1) were utilized to calculate warfarin concentrations.

Warfarin standard absorbance curve

Results

• Determining warfarin’s molar extinction coefficient

A warfarin standard absorbance curve was generated from samples of known concentrations in both water and hydrochloric acid (Fig. 1). The molar extinction coefficient for warfarin in water was calculated to be 12.8 x 10^-3 M^-1 cm^-1 (R²=0.99995). The molar extinction coefficient for warfarin in hydrochloric acid was calculated to be 8.5 x 10^-3 M^-1 cm^-1 (R²=0.99993).

• At low concentrations warfarin is stable

Since large concentrations of warfarin are not soluble in HCl solutions, it was dissolved first in water and then HCl was added to adjust the pH. We also detected two peaks of absorbance for warfarin in the low pH solution, but only one peak was observed in the high pH solution. With these two inconsistencies in mind, we decided to inquire whether warfarin concentrations were stable at low concentrations.

Our results suggest that warfarin is relatively stable at concentrations below 5 x 10^-3 M in high and low pH environments.

• Loss of warfarin occurs upon exposure to feeding tube

Our results support the argument that warfarin interacts with feeding tubes. When warfarin is in a low or high pH solution and introduced to feeding tube for one hour the concentration of warfarin decreases (Fig. 3). The percent of warfarin lost was 52.2% in water and was 58.5% in HCl. The original solution, which remained in a closed Erlenmeyer flask for one hour, did not display a significant loss in concentration, but rather as expected was very close to the original recorded concentration.

Figure 1: The chemical compositions of warfarin (A) and fluorescein (B) are similar.

Figure 2: Absorbance of warfarin (Å) and fluorescein (B) solutions before and after exposure to HCl using ultraviolet-visible (uv-vis) spectrometry, we estimate K of the reaction. Using fluorescein and calculate a lower limit of the equilibrium constant (K).

After fluorescein was exposed to feeding tube for one hour, its concentration decreased by 20.4% (Fig. 4A). In addition, the tube was cut into two pieces. One piece was not washed (Fig. 4B), while the other was washed once with water (Fig. 4C). Under ultra-violet light, an orange ring was observed on the inner surface of the unwashed tube; no fluorescence remained on the tube that had been washed.

• Quantifying the interaction between warfarin and feeding tube

Solutions, one after another, were then left in the same tube for 1 hour. Each of the four solutions was removed before the next was introduced. The concentration before and after an hour (Fig. 5), as well as the weight of tubing before and after, were then used to calculate a crude physical model of the equilibrium constant for this reaction, where [W] is the concentration of warfarin left in the feeding tube interface phase:

\[ W_{\text{final}} = W_{\text{initial}} - \frac{W_{\text{lost}}}{K} \]

\[ K = \frac{W_{\text{lost}}}{W_{\text{initial}} - W_{\text{final}}} \]

Figure 3: Absorbance of warfarin (A) and fluorescein (B) in 0.3 M HCl.

Figure 4: (A) Each bar represents the same fluorescein solution under different conditions: after one hour in glass and after one hour in feeding tube (B) Tube washed after fluorescein. (C) Washed after fluorescein.

Figure 5: This table was utilized to quantify the interaction. *Note: The moles above were calculated by dividing the molar concentration (M) by 1000.

Figure 6: The purple circles illustrate the concentration of warfarin left in the solution that was washed.

Conclusions

An interaction between warfarin and feeding tube is possible. Whether this interaction is due to the warfarin becoming physically trapped in the lumen, sticking to the lumen by means of an electostatic field or chemically adhering to the lumen has yet be determined and should be further investigated. As a drug that is widely used across the country, it is essential to understand how different methods of administering can hinder the bioavailability of warfarin, as well as other drugs.

Based on these results, warfarin should be administered through feeding tubes in high rather than low pH solutions. While this contradicts the recent study by Klang et al., the methods by which they observed the interaction possibly allowed the warfarin to bind to the both the lumen and outside of the feeding tube. As the outside of the feeding tube was not exposed to warfarin in our study and would not be significantly exposed to warfarin in the body, this could explain the discrepancy.

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