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## Summary

Due to excipient interference in the UV-detection of a sustained release gabapentin formulation, an alternative dissolution detection method using ninhydrin was evaluated. This method was determined to be linear, reproducible and accurate in the release rate determination of an ER gabapentin formulation.

## Introduction

Conventional analysis of gabapentin during dissolution is performed by UV-detection at 215nm. During the development of a novel 12 hour sustained release gabapentin formulation, it was found that certain raw materials and tablet excipients had significant absorbance at the 215 nm wavelength and consequently interfered with the detection and quantification of the gabapentin within the formulation. Therefore, a quick alternative method was necessary to accurately assess the release rate of gabapentin upon dissolution in order to support rapid formulation development.

Ninhydrin is a test reagent that reacts with alpha-amino acids to produce a purple color that can be detected at 402nm and 568nm. Previous work was performed by Wu, et al<sup>1,2</sup> to develop an assay to accurately assess the release rate of glucosamine from a sustained release matrix. This current work looks to assess the applicability of the ninhydrin assay to determine the release profile of gabapentin during dissolution.

## Experimental Method

### Dissolution setup and procedure:

Tablet dissolution was performed in a USP Type II apparatus at 50 rpm and 37°C. Dissolution medium was 900mL of deionized water (dH2O). Samples of 5mL each were automatically collected from each vessel at predetermined intervals, and the volume replaced with dH2O. After completion of the exam, a maximum dissolution determination was performed by increasing paddle speed to 250 rpm for 1 hour and collecting a final sample. Maximum absorbance values of tablets were used to calculate fractional release of the active ingredient.

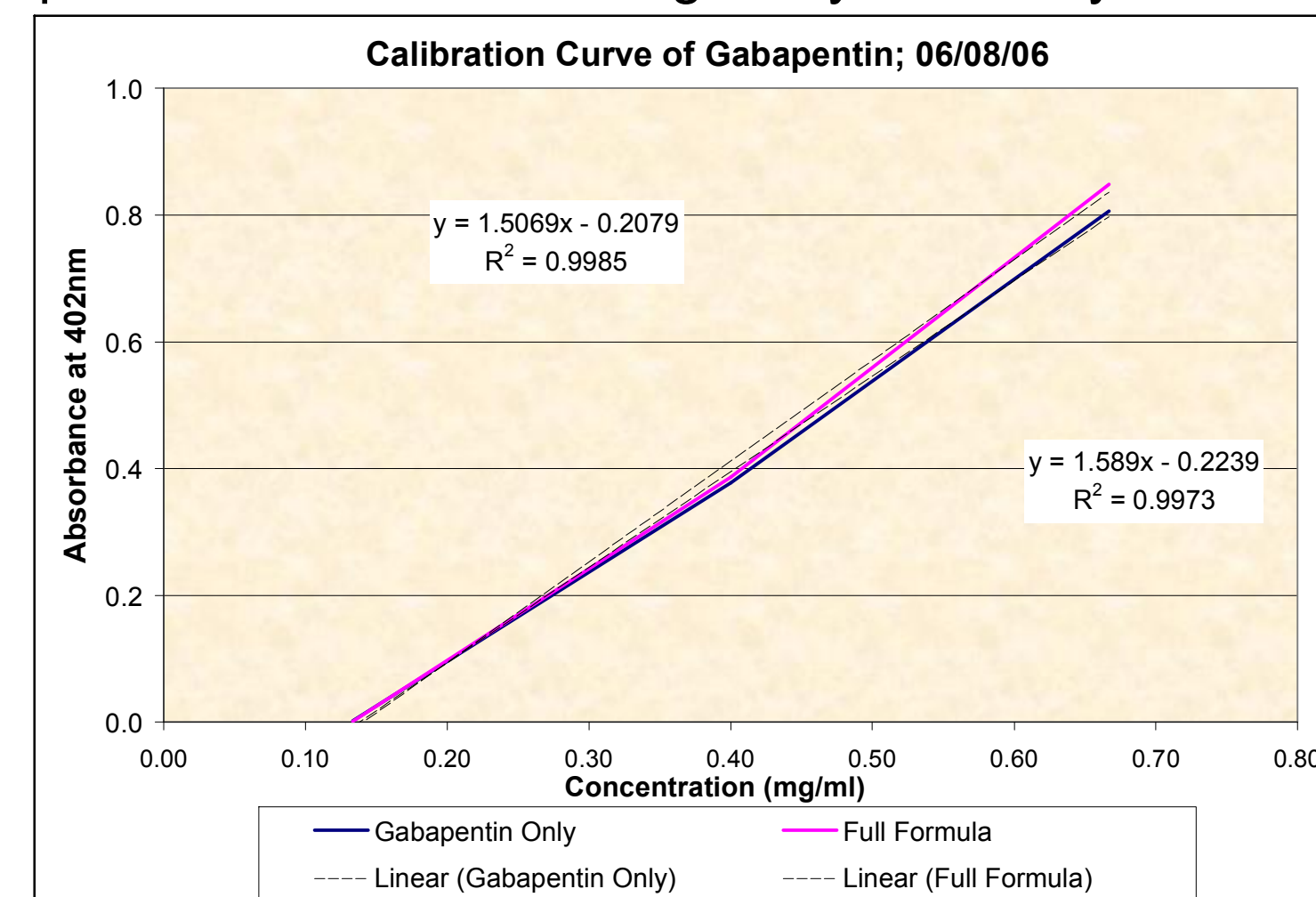
### Sample analysis and Gabapentin detection:

All samples were treated for Schiff's base formation as previously described<sup>1</sup>. 1.0mL of 0.8% ninhydrin solution and 0.5mL of 0.2M sodium phosphate buffer pH 6.0 were added to 5mL sample solution. These samples were heated at 85°C for 30 minutes, the reaction stopped by running under cold tap water. Samples were allowed to come to room temperature before detection. Detection was performed at 402nm and 568nm at appropriate dilutions for the linear range of the instrument.

## Results and Discussion

The gabapentin calibration curve, generated using the ninhydrin assay, is linear in the concentration range 0.13mg/ml – 0.70mg/ml. The gabapentin only calibration curve closely approximates the calibration curve of the full formula indicative of minimum excipient interference (Figure 1).

Figure 1. – Calibration curve of gabapentin performed on 6/8/06 using ninhydrin assay



Reproducibility of the method was evaluated by comparing the slopes generated over two different days. (Figure 2).

Figure 2. – Calibration curve of gabapentin performed on separate days using ninhydrin assay

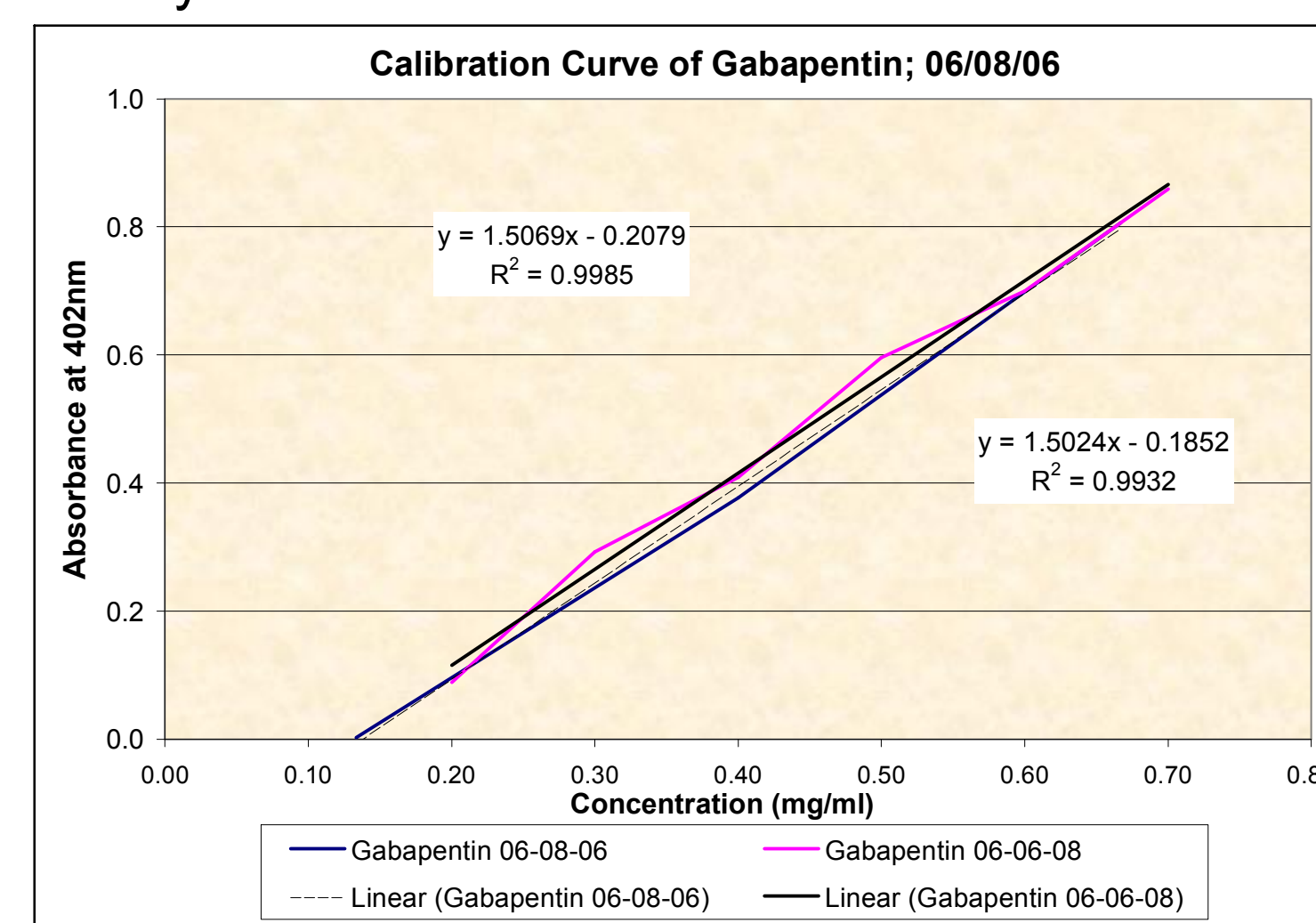
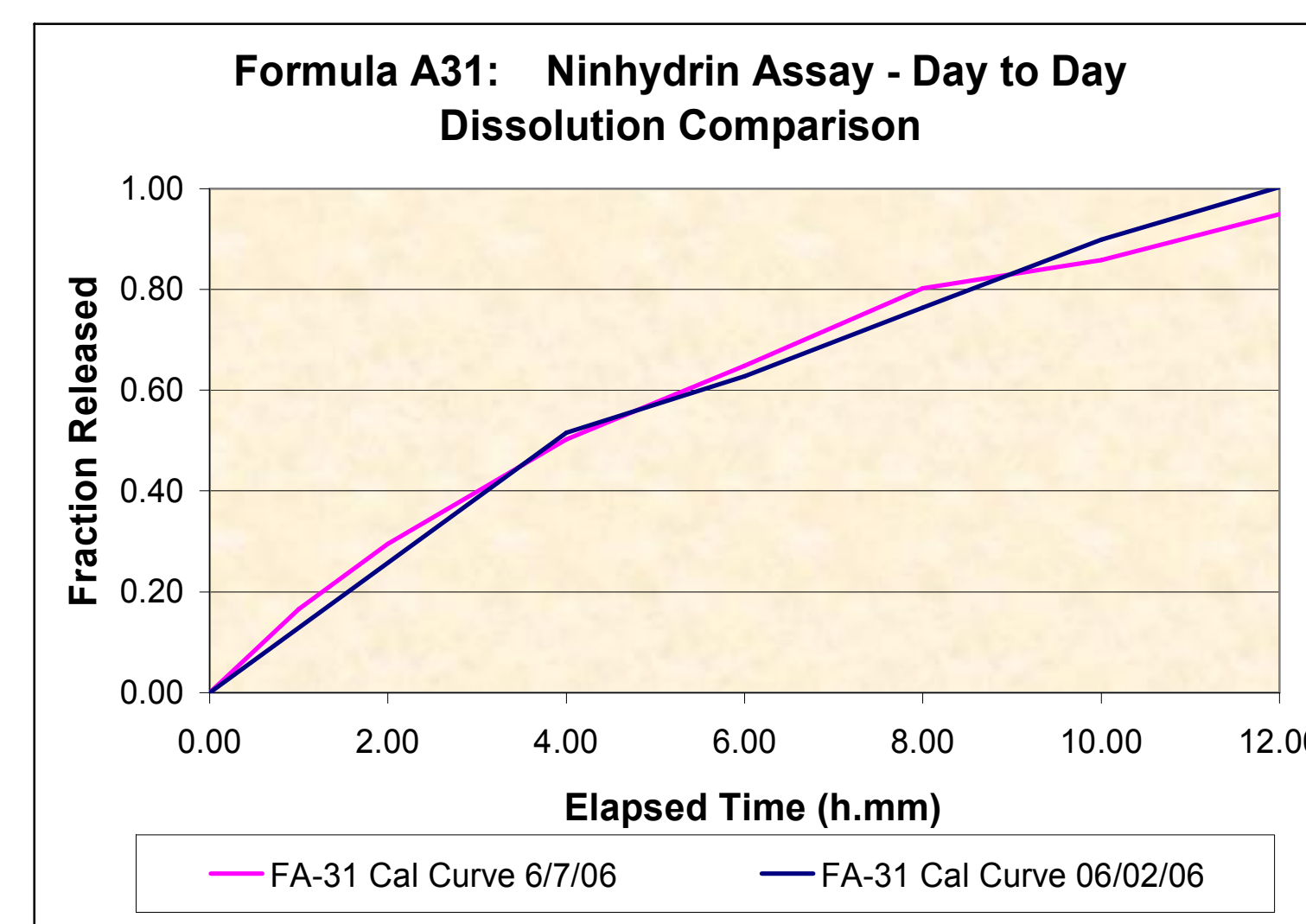


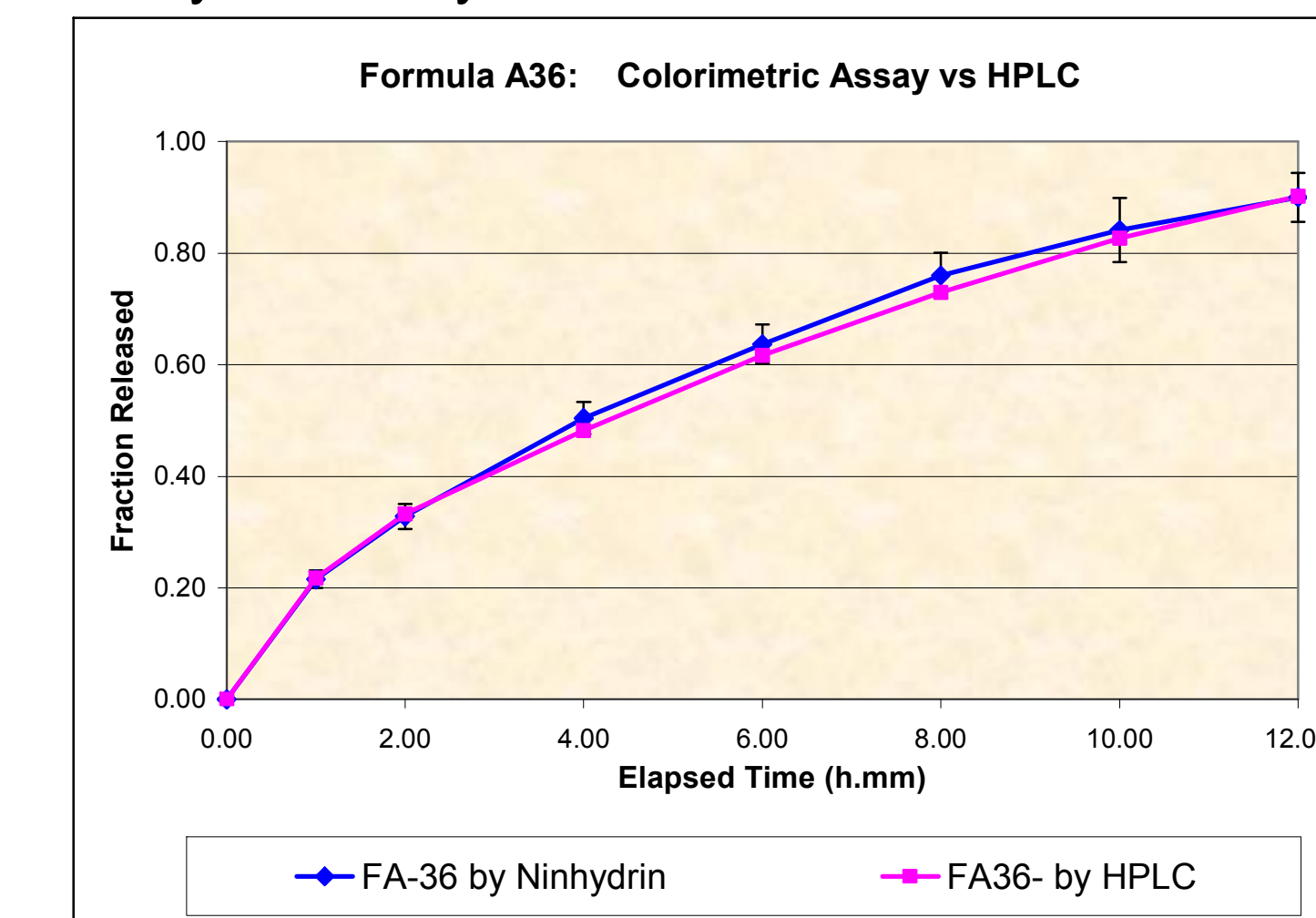
Figure 3 below shows the dissolution profile of gabapentin Formula A31 using the ninhydrin assay. Fresh calibration curves were used to produce dissolution profiles that were compared across two separate days. The release rates are essentially identical, indicating the ninhydrin method is reproducible.

Figure 3. – Day to day dissolution comparison of Formula A31 using the ninhydrin assay



Finally, the accuracy of the dissolution profile is confirmed with the UV analysis of gabapentin by HPLC. The release rate of gabapentin, determined by the ninhydrin assay is essentially identical to the release profile determined by HPLC analysis (as shown in Figure 4).

Figure 4. – Release rate of gabapentin by ninhydrin assay vs HPLC.



## Conclusion

The ninhydrin assay is a simple and reliable method for the determination of gabapentin in dissolution. The method corresponds well with HPLC sample analysis. The gabapentin calibration curve, generated using the ninhydrin assay, is linear within the dissolution concentration range of gabapentin and the method is reproducible from day to day.

## References

1. Y. Wu, M. Hussain, and R. Fassih. Development of a simple analytical methodology for determination of glucosamine release from modified release matrix tablets. *J. Pharm. Biomed. Anal.* 38(2): 263-269
2. Wu, Y., et al., *Unconventional Dissolution Method for Determination of Glucosamine From Sustained Release Matrix*; Dept of Pharmaceutical Sciences, Temple University School of Pharmacy, Philadelphia, PA 19140.

