



## Comparison of RP-HPLC and Non-aqueous Titration Method for Determination of Diphenhydramine Citrate and its Related Substances

L. CHEN<sup>1</sup>, X.Y. HE<sup>1</sup>, K. ZHOU<sup>1</sup>, D.F. LI<sup>1</sup>, T.L. LIU<sup>1</sup>, Z.H. WU<sup>2</sup>\* & Z.B. LI<sup>1\*</sup>

<sup>1</sup> College of Pharmaceutical Sciences, Southwest University, Chongqing, China

<sup>2</sup> Southwest University Hospital, Chongqing, China

**SUMMARY.** The RP-HPLC method was developed for simultaneous determination of diphenhydramine citrate, benzhydrol, and benzophenone on a Sepax HP-C18 column (4.6 mm x 250 mm, 5  $\mu$ m) at 258 nm. The mobile phase consisted of acetonitrile, water, and triethylamine (50:50:0.5, v/v/v, pH adjusted to 6.5 by phosphoric acid). The flow rate was 1.0 mL/min. The correlation coefficients between the peak area and concentration of each analyte were 0.9997 for diphenhydramine citrate, 0.9999 for benzhydrol and 1.0000 for benzophenone in ranges of 16.0~400.0, 2.0~50.0, 2.0~50.0  $\mu$ g·mL<sup>-1</sup> respectively. Non-aqueous titration method was also performed on determination of diphenhydramine citrate, and a good linearity between the sample weight and consumed titrant volume was obtained as the weight ranges from 0.2g to 1.6g (correlation coefficient: 1.0000). Both methods were accurate and precise for determination of diphenhydramine citrate. However, the RP-HPLC method, which could simultaneously detect impurities as benzhydrol and benzophenone, was more suitable for the quality control of diphenhydramine citrate.

**KEY WORDS:** Benzhydrol, Benzophenone, Diphenhydramine Citrate, Non-aqueous titration method, RP-HPLC.

\* Authors to whom correspondence should be addressed. *E-mail* addresses: lizhubo2007@163.com (Z.B. Li), wuzh@swu.edu.cn (Z.H. Wu).