2. Experimental

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2.1 Apparatus

Mettler-Toledo autotitrator DL 55 with Epson LX-300 pin writer, Mettler-Toledo Semi-micro Balance AG245. Waters Alliance 2690 Separation module with PDA 996 detector attached to a Dell Dimension XPS T500 computer with Waters Millennium^{32} software for total automated control of the instrument run, data acquisition, processing and report generation, Hanna Instrument 8521 pH meter and Millipore Elix 5 water purifying system (Type II water).

2.2 Materials and Reagents

Micronised grade of Loratadine was purchased from Angelini Acraf, Italy (Batch no: LRT0040). Potassium hydrogen phthalate and 0.1 N perchloric acid were purchased from Fisher Scientific; *di*-potassium hydrogen phosphate, phosphoric acid and glacial acetic acid from BDH Laboratory Supplies; HPLC grade methanol and acetonitrile from Merck.

2.3 Potentiometric Non Aqueous Titration

Glacial acetic acid was chosen as an amphiprotic solvent. Loratadine ionised in glacial acetic acid; conjugated base of acetic acid (Ac^-), was then titrated with perchloric acid.

150 mg of dried sample of Loratadine was weighed into 200-mL Polyethylene titration beaker. 50 mL of glacial acetic acid (auxiliary blank value determined) was added and stirred for 10 seconds to ensure complete sample dissolution.

The sample solution was titrated with standardised 0.1 N perchloric acid with potentiometry as equivalent point detection. Equivalent volume of titrant was determined by 1st derivative of E (mV) vs. V (mL) plot. A typical E vs. V and $\Delta E/\Delta V$ vs. V plot are shown in Figure 2 and Figure 3 respectively.

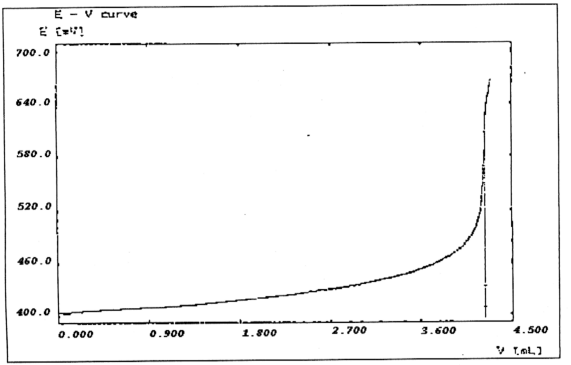

Figure 2: Typical E vs. V plot

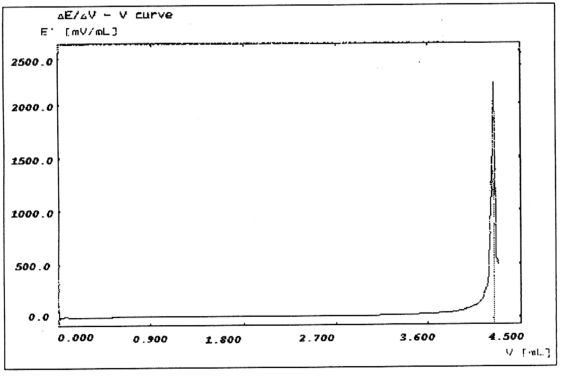

Figure 3: Typical ΔE/ΔV vs. V plot

2.4 RP-HPLC

A HPLC method using reverse-phase column (C_{18}) with phosphate buffer and acetonitrile as organic modifier was developed and the optimum conditions for the separation of Loratadine and its impurities are detailed as in Table 1.

Table 1: The optimum HPLC conditions for the separation of Loratadine and its impurities

Column	Novapak C_{18}, 4μm, 3.9×150mm with guard column
Mobile Phase	50:50 (%v/v) K_2HPO_4, 10mM, pH 7.70±0.05: Acetonitrile
Injection Volume	20μL
Temperature	Ambient
Test Solution's Concentration	0.10 mg/mL
Flow rate	1.0 mL/min
Detection wavelength	245 nm
Calibration	External, single point calibration. Assay standard concentration: 0.10 mg/mL Related substance standard concentration: 5μg/mL

The chromatography method was optimised with respect to its partition coefficient (k'), column efficiency (plate count, N) and peak tailing.

Table 2 shows the experimental values of these parameters obtained. Figure 4 shows the typical chromatogram of Loratadine (0.1 mg/mL)

Table 2: Experimental values of Column Performance and Separation Parameters

Parameter	Experimental value
Particient Coefficient, k'	5.9
Tangent Plate count, N	8420
Peak Tailing (USP)	1.47
Retention Time (minute)	9.6

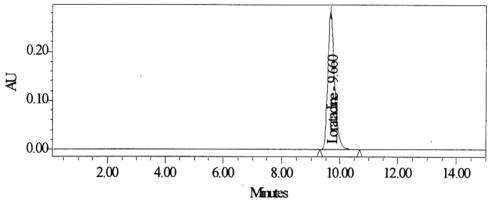

Figure 4: Typical Chromatogram of Loratadine (0.1 mg/mL)

The method developed has been validated with respect to specificity, linearity, accuracy, precision, intermediate precision (ruggedness) and robustness. Besides that limit of detection and limit of quantitation of the method was also determined.