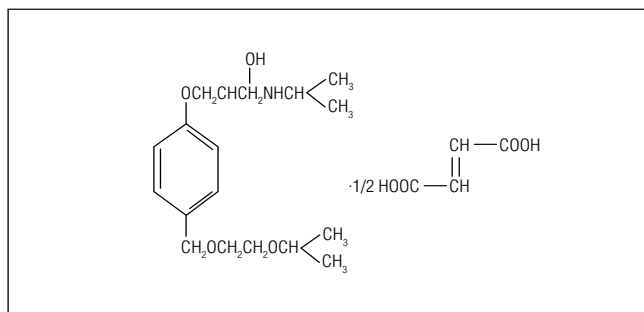


Simultaneous Separation of Bisoprolol and Its Counterion Fumarate

Bisoprolol fumarate is a synthetic β_1 -selective (cardioselective) adrenoceptor-blocking agent. Many drug substances are prepared as salts to promote solubility, improve stability, and/or improve bioavailability. For bisoprolol fumarate, bisoprolol is the active ingredient and fumarate is the counterion. Chemically, it is a 1-[4-[[2-(1-Methylethoxy) ethoxy] methyl] phenoxy]-3-[(1-methylethyl) amino]-2-propanol hemifumarate salt (structure shown below).



HPLC is usually only used to determine the active ingredient, bisoprolol, of bisoprolol fumarate.^{1,2} The simultaneous determination of its counterion, fumarate, has not been reported due to its weak retention on a conventional reversed-phase (RP) C18 column. The Acclaim® Mixed-Mode WAX-1 column, which combines anion-exchange and RP properties, has been used for determination of iodide in drinking water,³ corrosion inhibitors in engine coolants,⁴ additives in carbonated beverages,⁵ and simultaneous determination of a peptide and its acetate counterion.⁶ This column is a good choice for the simultaneous separation of bisoprolol and fumarate.

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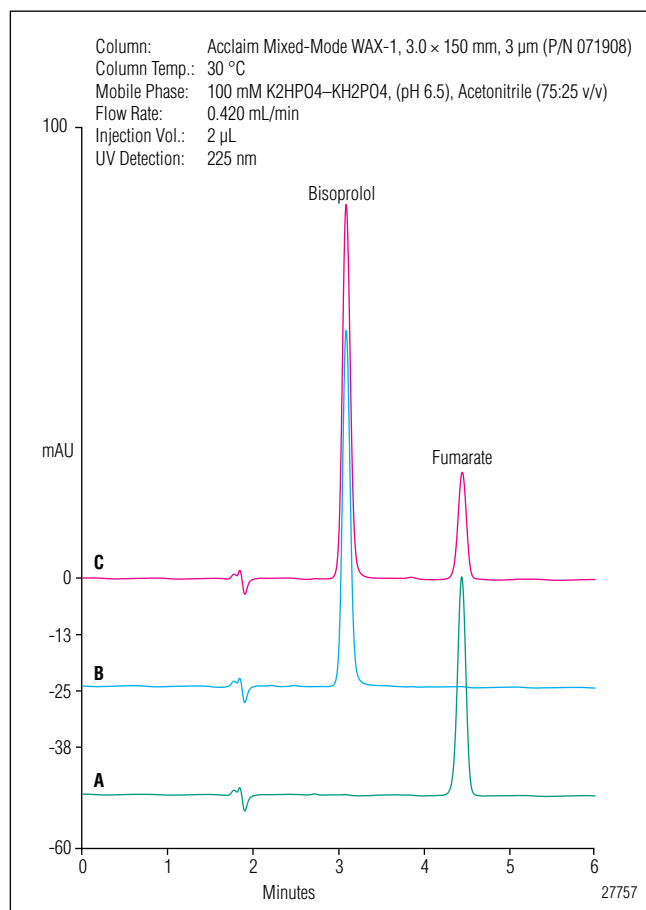


Figure 1. Overlay of chromatograms of A) fumarate standard (50 ppm), B) bisoprolol standard (100 ppm), and C) bisoprolol fumarate tablet.

The work shown here describes an efficient method for simultaneously separating bisoprolol and fumarate in a tablet sample. The method uses an Acclaim Mixed-Mode WAX-1 column (3.0 × 150 mm, 3 μm) with a phosphate buffer (100 mM of K₂HPO₄-KH₂PO₄, pH 6.5) and acetonitrile (75:25, v/v) mobile phase at 0.42 mL/min flow rate, and a detection wavelength of 225 nm. Figure 1 shows the overlay of chromatograms of a bisoprolol fumarate tablet sample and the standards. In a single injection, the analyst can determine both the active pharmaceutical ingredient and its counterion.

EQUIPMENT

Dionex UltiMate® 3000 Rapid Separation Liquid Chromatography (RSLC) system including:

HPG-3400RS Pump

WPS-3000RS Autosampler

TCC-3000RS Thermostatted Column Compartment

DAD-3000RS UV-vis Diode Array Detector

Chromeleon® Chromatography Data System (CDS) software Version 6.80 SR9

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