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Impurity profiling of varenicline tartrate by LC-QTOF mass spectrometric techniques during drug development

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Highlights

- 13 related substances in varenicline tartrate were characterized by LC-QTOF mass spectrometric method.
- Two related substances were synthesized and confirmed by NMR.
- The origins and formation mechanisms of related substances were determined.
- The obtained impurity profiles can provide references for quality control of varenicline tartrate.

Abstract

An LC-QTOF-MS method was developed for the separation and characterization of related substances in varenicline tartrate. The separation was established on an InertSustain C18 column (4.6 mm×150 mm, 5 μm) by liner gradient elution using 0.05% trifluoroacetic acid as mobile phase A and acetonitrile as mobile phase B. The degradation studies were conducted under the ICH prescribed stress conditions. Varenicline tartrate was found to be unstable to alkaline, oxidative, thermal and photolytic stresses, while relatively stable under acid stress condition. Thirteen related substances were detected all together in varenicline tartrate and its stressed samples. Their structures were identified mainly through positive ESI high resolution QTOF mass spectrometric analysis of the parent and product ions' accurate masses and the calculated elemental compositions. Among the 13 related substances, seven were process-related and six were degradation products, and two of them were further verified by chemical synthesis and NMR spectroscopic determination. Their formation