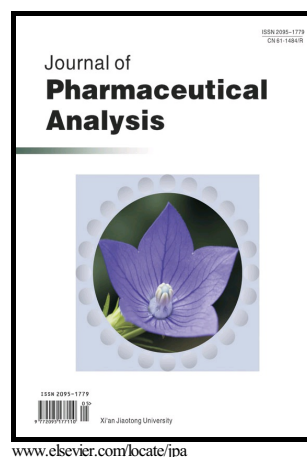


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Degradation kinetics of larotaxel and identification of its degradation products in alkaline condition

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ABSTRACT

Larotaxel, a new taxane compound prepared by partial synthesis from 10-deacetyl baccatin III, is active against tumors. In this research, a selective LC-MS method was developed and validated for the study of degradation kinetics of larotaxel, which was carried out in aqueous solutions with different pH (1.5, 3.0, 5.0, 6.5, 7.4, 9.0, 10 and 11.0) and temperature (0, 25, 37 and 45 °C). The linear range was 0.5-25 µg/mL, the intra- and inter-day precisions were less than 7.0%, and accuracy ranged from 97.4% to 104.5% for each analyte. The observed rate obtained by measuring the remaining intact larotaxel was shown to follow first-order kinetics. The activation energies for degradation were 126.7 and 87.01 kJ/mol at pH 1.5 and 11, respectively. Though larotaxel was stable in pH 5, 6.5 and 7.4 buffers at 37 °C for 24 h during our study, increasing or decreasing the pH of the solutions would decrease its stabilities. Moreover, three main degradation products in alkaline condition were separated by HPLC and identified by Q-TOF-MS. The three degradation products were confirmed as 10-deacetyl larotaxel, 7, 8-cyclopropyl baccatin III and 10-deacetyl-7, 8-cyclopropyl baccatin III.

Key words: Larotaxel; Degradation kinetics; pH; Temperature; Degradation products

1.Introduction

Cancer is still the leading cause of death throughout the world. While improved prevention and screening programmes will most likely contribute to a reduction in the

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