Stability-indicating HPLC Method for Determination of 7,8,9,10-tetrahydroazepino[2,1b]quinazolin-12(6H)-one, a Potential Anticancer Agent

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7,8,9,10-tetrahydroazepino[2,1b]quinazolin-12(6H)-one (TAZQ) (fig. 1), a synthetic analog of vasicine, has been reported to be an anticancer, bronchodilator, anti-inflammatory, antitussive, antiarthritic and antiasthmatic compound, which is under preclinical development for anticancer activity. The development of a validated reverse phase high performance liquid chromatography method is herein reported for the analysis and stability assessment. The analytical method was optimized using a C18 column and methanol:water (80:20 v/v) as mobile phase at flow rate of 0.9 ml/min. The eluents were monitored at 254 nm. Retention time of 7,8,9,10-tetrahydroazepino[2,1b]quinazolin-12(6H)-one was observed to be 3.9 min. It degraded significantly under alkaline conditions whereas negligible degradation was observed under acidic, oxidative, thermal and photolytic stress conditions. The peak of major degradation product, resulting from alkaline degradation, was well resolved from the peak of 7,8,9,10-tetrahydroazepino[2,1b]quinazolin-12(6H)-one. This method has been found to be linear, accurate, precise, robust, sensitive, specific, suitable and stability indicating.

Various metabolites that were detected did not show any bronchodilatory activity\textsuperscript{[10,11]}. TAZQ showed dose-related reduction in developing adjuvant arthritis in rats. It’s LD\textsubscript{50} was lower than 1000 mg/kg p.o, thus was safe at pharmacologically active doses\textsuperscript{[12]}. Structure activity relationship of TAZQ as bronchodilator has been studied extensively\textsuperscript{[7]}. It induced nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB)-mediated apoptosis in human colon carcinoma HCT-116 cell lines\textsuperscript{[13]}. A recent study, showed that its antiproliferative activity is through inhibition of PI3k/Akt/FoxO3a pathway\textsuperscript{[14]}.

Although TAZQ has been studied extensively for its biological activities and is currently in pre-clinical studies as anticancer agent (with reference to personal communication with PK-PD Division, IIIM-CSIR, Jammu, India), its stability indicating assay method has

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Fig. 1: TAZQ (7,8,9,10-tetrahydroazepino[2,1b]quinazolin-12(6H)-one).

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