Method validation

The PDA studies indicated that the method was sufficiently specific. The purity angle value was less than the threshold angle, indicating that the drug peak was pure by nature. The result of estimation and stress testing studies indicated a high degree of selectivity of this method. No interfering peaks were observed at the retention time of the analyte. The method provided adequate sensitivity for the determination of S002-853 in bulk drug substance and dosage forms. Precision of the assay was investigated with respect to both repeatability and reproducibility. The percentage RSD of assay S002-853 during assay method precision and in intermediate precision study were within acceptable limits (ICH 2003) confirming good precision of the method. The accuracy was also found to be within acceptable limits at all calibration points. The analytical method was found to be rugged with instrumental and environmental variation and also sufficiently robust within the range of tested conditions.

Table 3: Effect of pH on the compound S002-853

pH	R (correlation coefficient)	K (rate constant)	T_{50} (days)	T_{90} (days)
4	0.9960	3.066×10^{-2}	40.078	8.016
5	0.9945	2.153×10^{-2}	44.71	8.941
6	0.99997	2.0188×10^{-2}	51.170	10.234
7	0.9408	1.060×10^{-2}	76.79	15.36
8	0.96885	1.522×10^{-2}	59.09	11.818
9	0.9898	1.868×10^{-2}	50.524	10.105
10	0.9982	2.958×10^{-2}	38.80	7.76

Table 4: Temperature degradation of compound S002-853

Temperature (°C)	Reaction rate constant (K)	Half-life (weeks)	Shelf-life (weeks)
4*	0.0281	1779.35	355.87
25*	0.17456	286.43	57.28
37	0.3965	128.12	25.62
50	1.4715	34.73	6.946
60	1.8774	26.48	5.296

*Calculated

Physico-chemical parameters and stability studies

The solubility data indicate that the compound S002-853 is lipophilic in nature, and it is slightly soluble in water.

The samples of pH studies were collected at different days and analyzed by HPLC. The % remaining concentration was calculated from the calibration curves. The temperature degradation pattern of S002-853 was found to follow the zero order degradation, which indicated that the degradation of the compound is concentration independent. The rate constant (K), half-life ($t_{1/2}$), shelf-life (t_{10}) and energy of activation (E_a) at 25°C were calculated by LINREG. The % concentration remaining of S002-853 was found to be 23.87% in alkaline medium (0.1 N NaOH), 50.43% in acidic medium (0.1 N HCl), and 65.81% in 3% H_2O_2. In the drug excipients interaction, it was found that micro crystalline cellulose; lactose and magnesium stearate has no effect on S002-853. HPMC, EC and MC retard the release of the drug from the matrix [Figure 3].

CONCLUSION

The developed and validated HPLC method is reproducible and can be routinely used for QC of S002-853 in bulk

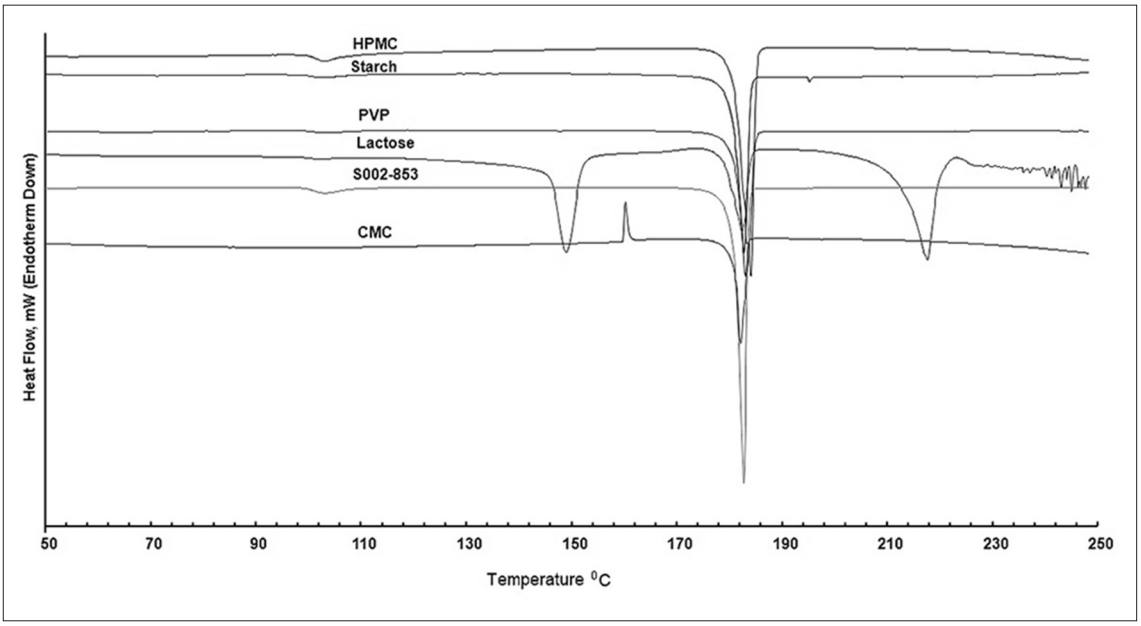

Figure 3: Differential scanning calorimetry of S002-853 with various excipients

manufacture, with ongoing stability studies for drug development process. Analytical studies were attempted on CDRI compound S002-853 to generate data beneficial for formulation development, further studies and Investigational New Drug application on the same. It provides base line separation of the compound of interest S002-853. The bulk samples of compound S002-853 from the Medicinal and Process Chemistry were checked by the above method. The results of stress testing undertaken according to the ICH guide lines reveal that the method is also selective and stability-indicating for S002-853. The solubility data indicate that the compound S002-853 is lipophilic in nature, and it is slightly soluble in water. The drug candidate is most sensitive towards alkaline condition as compared to acidic and oxidative conditions. The reported method can be very useful for further studies on bulk manufacture QC and in drug development process.

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