ABSTRACT

Saxagliptin (SAXA), a novel oral hypoglycaemic drug of the dipeptidyl peptidase-4 (DPP-4) inhibitor class, has initiated a new therapeutic approach for the treatment of type 2 diabetes mellitus. Currently, SAXA in combination with sulfonylurea (SUs) viz., glimepiride (GLIM), and glyburide is undergoing clinical trials. Both DPP-4 inhibitors and SUs, increase insulin secretion, produce synergistic effect, and thus suggest their utility in combination therapy.

A novel, simple, and applicable, reverse phase liquid chromatography (RP-HPLC) method was developed for the simultaneous estimation of SAXA and GLIM in tablet dosage forms, and biological samples. To achieve the best chromatographic separation of SAXA, and GLIM in the chromatogram, the mobile phase composition was optimized. The best optimized mobile phase composition, obtained for analytical method was, ACN (solvent A), and 0.1% sodium dihydrogen orthophosphate, pH 3.8 adjusted with orthophosphoric acid (solvent B) in the gradient mode. The gradient flow of solvents A and B, was in the order: A:B::30:70 for 0-2 mins, A:B::50:50 for 2-25 mins, and A:B::30:70 for 25-30 mins. On the other hand, the optimized mobile phase composition for the bioanalytical method was ACN (solvent A), and 10mM sodium dihydrogen orthophosphate, pH 3.8 adjusted with orthophosphoric acid, in the gradient mode. The gradient flow of solvents A and B, for bioanalytical method was in the order: B: 85-78% from 0-10 mins, B: 78-50% from 10-15 mins, B: 50% for 15-25 mins, B: 50-78% from 25-28 mins, and B: 78-85% from 28-30 mins. In each case, the optimized chromatographic conditions, furnished well resolved, sharp, and symmetrical peaks, for both the drugs i.e., SAXA and GLIM. The developed analytical, and bioanalytical methods, were found to be linear, accurate, precise, robust, suitable, sensitive, and specific, as per the regulatory guidelines. Further, the analytical method was successfully applied for the determination of the drugs in the tablets, which were developed in-house. Besides, the release kinetics of the SAXA and GLIM, from the tablet, was also studied employing the developed analytical method. Similarly, the developed bioanalytical method was successfully applied in the pharmacokinetic study of the SAXA, and GLIM tablets to evaluate pharmacokinetic parameters in wistar albino rats.

Key words: - Saxagliptin, Glimepiride, RP-HPLC, Validation, Simultaneous estimation, Rat plasma