DEVELOPMENT AND VALIDATION OF A NEW REVERSED-PHASE HPLC METHOD FOR THE SIMULTANEOUS DETERMINATION OF NIMESULIDE AND ITS IMPURITES IN DOSAGE FORMS

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Nimesulide (4-nitro-2-phenoxyethanesulfonanilide), a selective COX-2 inhibitor, has the potent anti-inflammatory and analgesic effects when administered orally, rectally, or topically. The aim of this study was to develop a stability-indicating HPLC method for determination of nimesulide and its impurities (2-phenoxyaniline and 2-phenoxy-4-nitroaniline) in different formulations of dosage forms. Some dosage forms consisted β-cyclodextrin which forms the inclusion complex with nimesulide. The lipophility of nimesulide and its impurities, which was determined by using ChemOffice 7 Ultra, is in good correlation with their HPLC behavior.

A simple, rapid, and specific reversed-phase HPLC method has been developed and validated for simultaneous determination of nimesulide and its impurities: impurity C (2-phenoxyaniline) and impurity D (2-phenoxy-4-nitroaniline) in raw material and dosage forms. Developed and validated method was applied for monitoring the stability of nimesulide in dosage forms. Compounds: 2-phenoxyaniline and 2-phenoxy-4-nitroaniline might be present in nimesulide dosage forms as a process-related impurities and degradation product respectively. The determination involved an isocratic elution of nimesulide and its impurities on a Agilent Zorbax Extend C₁₈ column at 40 °C (150 mm x 4.6 mm, 5μm) using a mobile phase: water:acetonitrile:TEA (55:45:0.4 v/v/v), pH adjusted to 5.2 with formic acid. The flow rate was 1.0 ml/min and the analytes were monitored at 230 nm. Under these conditions the retention time and retention factor were of 7.11 min and 4.21 for nimesulide; for 4-nitro-2-phenoxyethanesulfonanilide 7.98 min. and 4.85 and for 2-phenoxyaniline 8.66 min and 5.35, respectively. The presented results indicate that the investigated compounds were well separated with satisfied statistical parameters. The method was found to be linear in range from 15 – 150 μg/ ml for nimesulide and in range from 0.030 – 0.30 μg/ ml for impurities C and D.

All the validation parameters were within the acceptance range. The developed method was successfully applied for determination of nimesulide in different formulations of solid dosage
forms. The developed and validated method was suitable for application to stability studies of nimesulide and its impurities in investigated pharmaceuticals.