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RESEARCH ARTICLE

Validation of HPLC Method of Aceclofenac and Rabepazole Sodium in Aceclofenac Sustained Release and Enteric Coated Rabepazole Sodium Capsules

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ABSTRACT

The current research paper gives method validation report for the simultaneous quantification of Aceclofenac Sustained Release 200mg and Enteric Coated Rabepazole 20mg capsules. The method involved an isocratic system of Phosphate buffer pH 7.8 and methanol. The column used is Hypersil BDS C18 column with dimensions (250 mm* 4.6* 5µ). The compounds gave a good UV response at 280 nm, hence the detection wavelength. The developed method is simple, precise, robust and stands validated as per ICH guidelines.

Keywords: Hypersil BDS C18, methanol, RP-HPLC, Validation, Coated Rabepazole Sodium Capsules

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1. Introduction

Aceclofenac is a nonsteroidal anti-inflammatory drug (NSAID) analog of diclofenac. It is used for the relief of pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The drug works by inhibiting the action of cyclooxygenase (COX) that is involved in the International Journal of Chemistry and Pharmaceutical Sciences

production of prostaglandins (PG) which is accountable for pain, swelling, inflammation and fever. The incidence of gastric ulcerogenicity of aceclofenac has been reported to be significantly lower than that of the other frequently prescribed NSAIDs, for instance, 2-folds lesser than naproxen, 4-folds lesser than diclofenac, and 7-folds lesser

than indomethacin. Aceclofenac (C₁₆H₁₃Cl₂N₂O₄), chemically [(2-{2, 6-dichlorophenyl) amino} phenyl acetoxyacetic acid], is a crystalline powder with a molecular weight of 354.19. It is practically insoluble in water with good permeability. It is metabolized in human hepatocytes and human microsomes to form [2-(2',6'-dichloro-4'-hydroxy- phenyl amino) phenyl] acetoxyacetic acid as the major metabolite, which is then further conjugated. According to the Biopharmaceutical Classification System (BCS) drug substances are classified to four classes upon their solubility and permeability. Aceclofenac falls under the BCS Class II, poorly soluble and highly permeable drug.

Rabeprazole is a proton pump inhibitor that suppresses gastric acid production in the stomach. It has several medical uses: the management of conditions that involve excess gastric acid production (e.g. Zollinger–Ellison syndrome), conditions that are worsened by gastric acid (e.g. ulcerations of the gastrointestinal tract), and conditions involving prolonged exposure to gastric acid (e.g. symptomatic gastro esophageal reflux disease).

Rabeprazole's adverse effects tend to be mild but can be serious, including deficiencies in essential nutrients, rare incidences of liver and bone damage, and dangerous rashes. Rabeprazole can theoretically contribute to numerous drug interactions, mediated both through its metabolic properties and its direct effect on acid in the stomach, though its potential for clinically meaningful drug interactions is low. Like other medications in the proton pump inhibitor class, rabeprazole's mechanism of action involves the permanent inhibition of proton pumps in the stomach, which are responsible for gastric acid production. Rabeprazole has a number of chemical metabolites, though it is primarily degraded by non-enzymatic metabolism and excreted in the urine. Genetic differences in a person's drug-metabolizing enzymes may affect a person's response to rabeprazole therapy, though this is unlikely in comparison to other proton pump inhibitors. Rabeprazole is marketed around in the world in a variety of combinations and brand name products. Aceclofenac Sustained Release 200mg and Enteric Coated Rabeprazole 20mg are in Capsule form. The analytical method for Aceclofenac and Rabeprazole Sodium Assay is a reverse phase HPLC method. During method validation; Specificity, Precision, Linearity, Range, Robustness, and System Suitability Test parameters will be carried out.

2. Materials and Methods

Dipotassium hydrogen phosphate AR grade, Orthophosphoric acid HPLC grade, Methanol HPLC grade and Purified water were procured from Merck India Pvt Ltd. Sodium lauryl sulphate AR grade was procured from Sigma Aldrich.

Chemical and Standard Solution Preparations

Standard Resolution Solution: About 200 mg of Aceclofenac & 20 mg of Rabeprazole Sodium working

standard were weighed and transferred in 100 ml volumetric flask. To this 20 ml of methanol was added and kept for sonication for about 10 minutes. Further addition of 50 ml of buffer pH 7.8 + 0.5% SLS was done and sonicated for about 5 mins. Ice cubes were into water of Sonicator bath to avoid rise in temperature due to sonication. Final dilution was done with buffer pH 7.8 + 0.5% SLS. 2 ml of the above stock solution was diluted to 50 ml with mobile phase. This is the resolution solution for assay & the system suitability standard. The resolution between Rabeprazole peak (major peak 1) & Aceclofenac peak (major peak 2) is not less than 2.0. Inject 20 µl of this solution onto the system under the conditions mentioned above and calculate content of Aceclofenac and Rabeprazole Sodium

Sample Solution

The contents of 5 capsules were weighed and transferred in a 250 ml beaker. About 80ml of methanol was added and the solution was sonicate for about 15 to 20 minutes. Ice cubes were into water of Sonicator bath to avoid rise in temperature due to sonication. About 100ml of buffer pH 7.8 + 0.5% Sodium lauryl sulfate was added and sonicate further for about 10 minutes. The solution was quantitatively transferred to 500 ml volumetric flask. To this solution 20 ml methanol was added for the foam to subside and volume was made upto the mark using buffer pH 7.8 + 0.5% Sodium lauryl sulfate. This solution was centrifuged at 3500 rpm for 5 minutes. 2ml of centrifuged solution was diluted to 50ml volume with mobile phase.

Table 1: Instrumentation and Chromatographic Conditions

| Parameter | Description |
|----------------------|---|
| Instrument | Shimadzu UFLC Prominence System |
| Pump | LC – 20 AD binary pumps |
| Injector | Autosampler (SIL – 20 AC HT) |
| Injection volume | 20 µl |
| Column oven | CTO – 20 AC at 25°C |
| Column | Hypersil BDS C18 (5 µ * 4.6 mm id * 250 mm) |
| Mobile Phase | Isocratic system of Phosphate buffer pH 7.8 : methanol (40: 60) Run time: 10 min. |
| Flow Rate | 1.5 mL/min |
| Detector | UV Detector- UV-4075 |
| Detection Wavelength | 280 nm |

Method Validation

System Suitability

System suitability tests were carried out to ensure reproducibility of the equipment. The test was carried out by injecting standard solution in 5 replicates, single injection of blank solution and test solution.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of other components which may be

expected to be present. The tests were carried out by injecting diluent blank, Resolution Standard Solution, Placebo Solution of Rabeprazole Sodium, Placebo solution of Aceclofenac (Rt 7.092 min), Rabeprazole Sodium (Rt 3.852 min) Standard Solution, Aceclofenac Standard Solution, Placebo + Standard Solutions, Sample Solution.

Precision

Precision is the measure of either the degree of reproducibility or of repeatability of the analytical method under normal conditions. The test was carried out with 6 assay samples in replicate injections of standard solutions.

Linearity

The linearity of an analytical procedure is its ability to obtain test results which are directly proportionally to the concentration of analyte in the sample. Linearity of Aceclofenac and Rabeprazole Sodium was carried out at 50, 75, 100, 125 and 150% of working level of Aceclofenac and Rabeprazole Sodium.

Ruggedness

Ruggedness expresses within laboratories variation in terms of different days, different analyst, different equipment, etc. Different analyst performed the analysis using fresh standard and sample solution on different days and equipments. The conditions applied here were by carrying out 5 replicate analysis solutions at 275 nm, by using buffer of pH 7.0: MEOH (40: 60 v/v), buffer of pH 7.4 : MEOH (40 : 60 v/v), buffer of pH 7.8 : MEOH (44 : 56 v/v), buffer of pH 7.8 : MEOH (36 : 64 v/v), flow rate 1.3 ml/min and flow rate of 1.65 ml/min.

3. Results and Discussions

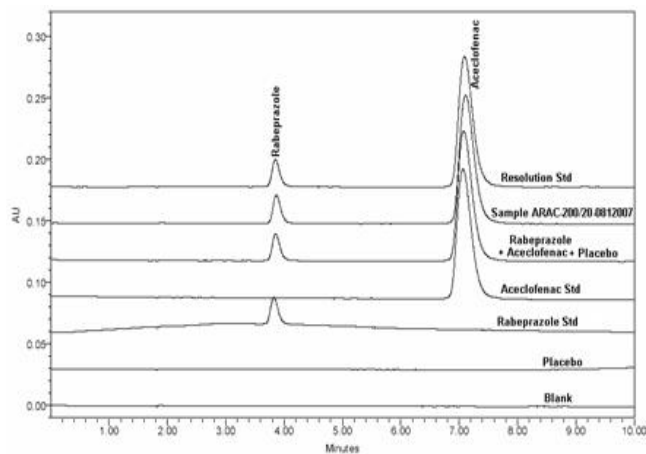


Figure 1: Chromatogram overlay

System Suitability

The method was found to be suitable for the proposed analysis as the relative standard deviation of average peak area of system suitability test is not more than 2.0 %

Specificity

Retention time obtained with test sample is comparable to the retention time obtained for the standard. All peaks are well separated from each other indicating the specificity of the analytical method for Rabeprazole Sodium and Aceclofenac.

Precision

Precision measured at all level was within the acceptable criterion of NMT 2.0 % indicating the efficiency of method for the proposed analysis.

Robustness

The method was found to be robust as all the parameters applied produced result with an acceptance criterion of RSD NMT 2.0 %.

4. Conclusion

The method developed for simultaneous analysis of Aceclofenac and Rabeprazole Sodium stands to be validated as per ICH guidelines. The limits for all the parameters were met with no interference from the placebos of the capsules and hence this method can be used as quality control tool for analysis of the capsules.

5. References

- [1] ICH Harmonized Tripartite Guideline prepared within the Third International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH), Validation of Analytical Procedures: Methodology, 1996.