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A Review on – Development and Validation of Stability-Indicating RP-HPLC Method for the Determination of Nabumetone

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ABSTRACT

Analytical method development and validation is the integral part of drug sighting and development of drug substance in pharmaceutical preparations. Analytical method is the method which determines drug contented, impurities existence and degraded products and validation gives proof for the developed method is truthful and used in quality control process. Designing of new analytical method useful in enhancement of precision, exactness, cost and time consumption for analysis. The developed method was based on RP-HPLC leave-taking and quantification of the drug on C-18 column using a mobile phase at flow rate of 1 ml/ min. Quantitation was attained with PDA detector at 200-400 nm based on peak area with linear calibration curves at concentration ranges 5-25 µg/ml for the drug. The method had been successively functional to pharmaceutical formulation. No chromatographic intrusion from the tablet ingredients was introduced. The developed method was verified for linearity, recovery and specificity. The intra and inter-day precision and accuracy values had been withinside the recognition variety as consistent with ICH guidelines.

KEYWORDS: Nabumetone, NSAID, RP-HPLC, Method validation.

I. INTRODUCTION

Nabumetone [1] is non acidic prodrug, chemically, 4-(6-methoxy-2-naphthyl)-2-butanone [1], NSAID of 6-Phenylhexanoic acid group accustomed to contend ache and inflammation induced by rheumatism.[1] The literature survey discloses that colorimetric [3] and some chromatographic systems had been reported for the analytical assay of nabumetone in various fluids like biological fluids and in medicinal preparations besides alone or other drugs. [5-6]

According to previous study Non-Steroidal Anti-Inflammatory Drugs (NSAIDs),[2] Nabumetone's is an active metabolite which constrains the cyclo-oxygenase enzyme favorably blocks the activity of COX-2 (Cyclo-Oxygenase - 2). During arthritis, cyclo-oxygenase-2 enhances the rate of production of endoperoxides and prostaglandins E-2 and I2 (prostacyclin) which is indirectly responsible for severe pain in the patients. Nabumetone (NAB) comes under a new class of non-steroidal anti-inflammatory drug which show less potential for GI sheath irritancy and inhibits the function of platelet. It shows less impact not only on nephric bradykinin emission but also on congestive heart failure (CHF) as compared to other old drugs of this class.[4]

There are some articles available describing investigative procedures for NAB. This review paper describes the easy, precise and delicate HPLC technique which is recuperated and attested(documented) method for estimation of NAB as per ICH (International Conference on Harmonization) guidelines. Here, we review offered novel technique for the decisiveness of NAB which utilizes a very economical solvent system on a Waters ODS C18 analytical column. This type of system primes to improved preservation, very serrated and proportioned peak figures and displays fine selectivity for Nabumetone.[7]

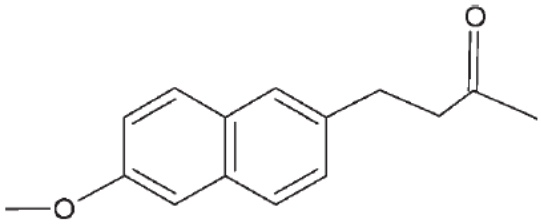

Figure 1. Structure of Nabumetone

II. INSTRUMENTATION:

A SHIMDZU AHT HPLC system containing of PV-980 pump, a 975 UV-Visible detector was used. The peaks were measured through a PC based Class-VP software.[7]

Chromatographic Conditions:

A reverse phase C18 column-based chromatography was balanced with mobile phase combination of ethanol, acetonitrile, H2O, ammonium acetate, Potassium dihydrogen phosphate, Triethylamine and oxyacid, Tetra butyl ammonia water sulphate (TBAH) of HPLC grade with different concentration ratios.[5,10,11] E.g., Acetonitrile: water (80:20 %v/v)[10], Ethanol: water (30:70 %v/v)[5], Acetonitrile: H2O (50:50 %v/v)[4], etc. Mobile phase rate of flow was maintained at 1 ml/min and effluents were monitored at 200-400 nm. The sample was injected employing a 10 µl fixed loop system and therefore the total run time was 10 min.[4,5]

Preparation of mobile phase and stock solution

a) Weigh 25 mg and transferring analytically pure Nabumetone to 25 ml volumetric flask, volume was made up to the mark (25 ml) with diluent (Acetonitrile and Water 50:50 %v/v), which gave 1000 µg/ml of the drug. the answer was further diluted with the identical diluent to get final concentration of 100 µg/ml.[4]

b) The quality stock solutions of Nabumetone (Nabumetone) (100 µg/ml) were prepared by dissolving appropriate amounts of drug compounds in acetonitrile, whereas within the preparation of sample solution, quantity of powdered tablet akin to 10 mg of Nabumetone was weighed and dissolved in acetonitrile. it absolutely was further diluted so as to urge solution having concentration 50 µg/ml of drug.[9]

Methodology For Sample Solution (Study of Marketed Preparation)

Twenty tablets were counted and finely pulverized. Powder equal to twenty-five mg Nabumetone became as it should be weighed and transferred to a 25 ml volumetric flask and 20 ml of Acetonitrile became delivered to the identical. The beaker was sonicated for 20 min and volume was made up to the mark with Acetonitrile. The below result was filtered using Whatman sludge paper (No. 1) (11µm). Applicable volume of the aliquot part was transferred to a 25 ml volumetric beaker and the volume was made up to the mark with mobile phase to gain 100 µg/ ml of Nabumetone. The result was sonicated for 10 min and fitted under above chromatographic conditions, the chromatogram was recorded and the peak area was measured.[4]

III. METHOD VALIDATION

The freshly developed RP-HPLC method was validated in terms of precision, accuracy, linearity, robustness, specificity in keeping with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines.[15]

Linearity: The calibration curve was drawn by plotting nabumetone average area for triplicate injections and therefore the concentration expressed as a percentage. Linearity was checked over the identical concentration range for 3 consecutive days. Good linearity was observed within the concentration range from 3-80 µg/ml of nabumetone. Linear calibration plots for nabumetone were obtained over the calibration range and by calculating the corresponding equation. The standard curve was calculated by linear regression method: $y=ax+b$, where y is the peak area ratio of drug to internal standard, a and b are constant, and x is the nabumetone concentration (ng/ml). [11,12,13]

Specificity: Stress studies of the drug's active pharmaceutical ingredients were utilized for the identification of the possible degradation products and for the validation of the stability-indicating analytical procedures. Specificity is that the ability of the analytical method to live the analyte concentration accurately response within the presence of its all-potential degradation products. Specificity of the tactic towards the drug was studied by determination of purity for drug peak in stressed sample employing a PDA detector. The study of resolution factor of the drug peak from the closest resolving degradation product was also done. Both drug and degradation product peaks were found to be pure from peak purity data.[8,10,11]

System suitability: A system suitability test was performed to judge the chromatographic parameters before the validation runs. The system suitability parameters with relevancy theoretical plates, capacity factor, resolution factor, tailing factor is calculated.[10,11]

Precision: Precision of the tactic was verified by intermediate and repeatability precision studies. The intra-day (Repeatability studies) includes six independent solutions which are observed in single sooner or later at various time (e.g., 15, 30, 45, 60, 90, 120, etc.) and therefore the inter-day precision study (Intermediate studies) involves study of over two days.[4,8,10,11]

Accuracy: Accuracy of the tactic was evaluated by injecting a combination of strained samples with three known concentrations of nabumetone, viz., 10, 20 and 30 µg/mL, in triplicate so defining the percent recovery of the further extra drug. the share of added API attained from difference between peak areas of unshielded and shielded samples of nabumetone. the proportion recovery of nabumetone within the bulk drug samples ranged from 91.6 to 97.3%, respectively.[8,10,11,13,]

LOD and LOQ: The LOD is that the lowest limit and therefore the LOQ is that the lowest concentration which will be quantitatively measured supported the S.D. deviation of the response and therefore the slope.[8,10]

Robustness: Altogether the deliberately varied chromatographic conditions (e.g., rate and UV detector wavelength), the chromatogram for system suitability showed satisfactory resolution (%RSD<2) with no significant changes in chromatographic parameters.[8,10]

V. RESULTS AND DISCUSSION

This study represents an easy and validated RP-HPLC method for estimation of nabumetone within the presence of degradation products. The developed method is particular, accurate, precise and robust. All the degradation products formed during forced decomposition studies were well separated from the analyte peak demonstrating that the developed method was specific and stability indicating. the tactic may be applied successfully even to the analysis of marketed products nabumetone tablet formulation, as no interference was observed because of excipients or other components present.

VI. CONCLUSION

The easy, precise and delicate validated RP-HPLC method for instantaneous determination of two-component drug mixture of Nabumetone and Paracetamol has been established. the tactic is also suggested for routine and internal control analysis of the investigated drugs in pharmaceutical formulations.

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