Development and validation of RP - HPLC method for the estimation of frovatriptan succinate in bulk and tablet dosage form

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Received on:10-11-2011; Revised on: 15-12-2011; Accepted on:12-01-2012

ABSTRACT
A simple, accurate, precise RP -HPLC method was developed and validated for the determination of frovatriptan succinate in Pharmaceutical dosage form. Separation was achieved under optimized chromatographic condition on a Kromasil C18 (ODS) column (250 X 4.6 mm i.d., particle size 5µ). The mobile phase consisted of Methanol: Phosphate buffer at pH 3.2: Acetonitrile in the ratio 50: 40:10v/v. An isocratic elution at a flow rate of 0.8 ml/min at ambient temperature. The detection was carried out at 244nm using Waters HPLC 515-UV-Visible detector (2487). The retention time of frovatriptan is found to be 3.5min and the calibration curve was linear in the concentration range of 5–30µg/ml (r2- 0.9997). The limit of detection and the limit of quantification were found to be 0.323 and 1.632µg/ml respectively. The amount of frovatriptan present in the formulation (Frova) was found to be 99.59%. The method was validated statistically using the SD, %RSD and SE and the values are found to be within the limits and the recovery studies were performed and the percentage recoveries was found to be 99.61± 0.3528 %. So, the proposed method was found to be simple, specific, linear, and rugged. Hence it can be applied for routine analysis of frovatriptan in the Pharmaceutical formulations.

Key words: Frovatriptan succinate; HPLC; bulk and Tablets; Validation.

INTRODUCTION
FROVA (frovatriptan succinate) tablets contain Frova (frovatriptan succinate) triptan succinate, a selective 5-hydroxytryptamine (5-HT1B/1D) receptor subtype agonist, as the active ingredient. Frova (frovatriptan succinate) triptan succinate is chemically designated as R(+)-3-methylamino-6-carboxamido-1, 2, 3, 4-tetrahydrocarbazole monosuccinate monohydrate and it has the following structure. It is newer drug used in the treatment of for the treatment of migraine headaches. The review of literature revealed that no methods were reported for the estimation of frovatriptan in bulk and tablet formulations.

EXPERIMENTAL METHODS: Instrumentation and analytical conditions:
The validated method utilized a Waters HPLC 515-UV-Visible detector (2487) with an isocratic elution technique at a flow rate of 0.8 ml / min on a Kromasil C18 column (250 X 4.6 mm i.d., 5µ) at ambient temperature. The mobile phase consisted of Methanol: Phosphate buffer at pH 3.2: Acetonitrile in the ratio 50: 40:10v/v. An isocratic elution at a flow rate of 0.8 ml/min at ambient temperature. The UV detection wavelength was at 244 nm (fig.02). The retention time for frovatriptan was found to be 3.5 minutes.

Fig.1.Chemical structure of frovatriptan

Fig.2.Absorbance Spectrum for frovatriptan.

Stock and working standard solutions:
Stock standard solution of 1000µg/ml of frovatriptan was prepared freshly by accurately weighing 25mg of frovatriptan into 25ml volumetric flask. Dissolved and made up to the volume with Phosphate buffer (pH 3.2). Further diluted by pipetting 1ml into 25ml volumetric flask to obtain 100 µg/ml solution. The solution was further diluted with mobile phase in 10ml
volumetric flask to obtain six working standards in the concentration range 5-30 µg/ml of frovatriptan (fig. 03). Chromatogram was recorded thrice for each dilution. All the solutions were prepared in triplicates.

**Assay of sample preparation:**

Twenty commercial tablets (frova Tablets contain labeled concentration 100 mg of frovatriptan) were weighed and their mean mass was determined. After grinding the tablets into a fine powder in a glass mortar, an accurately weighed quantity of the tablet powder equivalent to 25 mg of frovatriptan was quantitatively transferred into a 25 ml volumetric flask with about 20 ml of phosphate buffer pH 3.2. The solution was sonicated for 10 min, brought to the volume with phosphate buffer, mixed well and 1 ml of filtered test solution was transferred into 25 ml volumetric flask and made up to the volume with mobile phase (40 µg/ml). 1.5 ml aliquot solution was transferred into a 10 ml volumetric flask. The theoretical frovatriptan concentration after dilution was 30 µg/ml (100% of frovatriptan). An aliquot of this solution was filtered through a 13 mm membrane syringe filter (Pore size 0.2 µm) prior to the injection into the HPLC system. Peak area of frovatriptan was measured for the determinations (shown fig. 04).

Finally the method was validated as per ICH guide lines for precision, accuracy, specificity, linearity, reproducibility, LOD and LOQ. Sample solution short term stability was tested at ambient temperature (20 ± 1°C) for 3 days.

**RESULTS AND DISCUSSION**

A simple, selective, rapid, accurate, precise RP-HPLC method for the estimation of frovatriptan in bulk and tablet dosage form has been developed and validated. The linearity range was determined by external standard calibration method in the concentration range of 5-30 µg/ml ($r^2$ - 0.9997). It indicated that the concentrations of frovatriptan had good linearity. The LOD and LOQ were found to be 0.323 and 1.632 µg/ml respectively. The system suitability parameters like capacity factor, asymmetric factor, tailing factor, HETP and no. of theoretical plates were tested. The amount of frovatriptan was calculated as 99.55%. And it was observed that all the values are within the limits. Further the precision of the method was confirmed by the repeatable analysis of formulation. The % RSD was found to be 99.61 ± 0.3528 %. It indicated that the method has good precision. The low % RSD value indicated that there is no interference due to excipients used in formulation. Hence, the accuracy of the method was confirmed.

**CONCLUSION**

The developed RP-HPLC method was validated and the system suitability studies were performed and all parameters combined with the simplicity and ease of operation ensures that the validated method can successfully used for routine analysis of frovatriptan tablet dosage formulation.

**REFERENCES**


Source of support: Nil, Conflict of interest: None Declared