ISSN 0250-474X
May - June 2015
77(3) : 249-366

Indian Journal of Pharmaceutical Sciences

Scientific Publication of the Indian Pharmaceutical Association

Indian Pharmaceutical Association IPA
1939-2014 Platinum Jubilee
Crusade for the Profession

Medknow
Wolters Kluwer
PubMed
Impact Factor® for 2013: 0.296
www.ijpsonline.com

A Stability Indicating HPLC Method for the Determination of Nitisinone in Capsules

EFFAT SOURI*, FARNAZ R. LAHIJI[1], TANNAZ NOURHASHEMI[1] AND H. JALALIZADEH[2]
Department of Medicinal Chemistry, Faculty of Pharmacy and Drug Design and Development Research Center, Tehran University of Medical Sciences, Tehran-14155-6451, [1]School of Pharmacy, Tehran University of Medical Sciences, International Campus, Tehran, [2]Department of Research and Development, Osvah Pharmaceutical Co. Tehran, Iran

In this study a simple and efficient stability-indicating HPLC method with short run time was developed for the determination of nitisinone. The stress degradation of nitisinone was studied in different acidic, basic, oxidative, thermal and photolytic conditions. The chromatographic separation was achieved on a Nova-Pak C18 column using a mixture of 50 mM NaH_2PO_4 (pH 2.5) and acetonitrile (45:55, v/v) as mobile phase. UV detection was performed at 280 nm. Good linearity was observed over the concentration range of 0.5-50 μg/ml with r^2>0.999. The within-day and between-day precision values were less than 2%. The proposed method could be used for the determination of nitisinone in the presence of its degradation products and also dosage form excipients for the quality control purposes.

Key words: Nitisinone, stability-indicating, stress degradation, HPLC, UV detection

Nitisinone (NTBC), 2-(2-nitro-4-trifluoromethyl benzoyl)-1,3-cyclohexanedione (fig. 1), is a reversible inhibitor of 4-hydroxyphenylpyruvate dioxygenase, which is used for the treatment of hereditary tyrosinemia type I[1]. Only a few articles have been published which reported the HPLC determination of nitisinone in biological fluids[2,3]. Capillary electrophoresis[4] and LC-MS/MS methods[5-9] have also been reported for the determination of nitisinone in biological samples. There is no pharmacopeial monograph for nitisinone or any reported HPLC method for the determination of nitisinone in pharmaceutical dosage forms.

In this study an HPLC method has been developed and validated for the determination of nitisinone in pharmaceutical formulations, which is necessary for quality control purposes. The stability of nitisinone was also studied under different stress conditions and the proposed method was shown to be stability-indicating.

Nitisinone bulk powder (batch No: 9009011) and nitisinone capsules (2 mg) (Batch No: 007) were kindly provided by Osvah Pharmaceutical Company, Tehran, Iran. All the analytical grade chemicals and HPLC grade solvents were from Merck (Darmstadt, Germany). Water was purified by using a Milli-Q purification system (Millipore, Milford, MA, USA). Stock standard solution of nitisinone at the concentration level of 2500 μg/ml was prepared in methanol. Working standard solutions were freshly prepared by consecutive dilution in mobile phase during the analysis day.

A Waters HPLC system (Milford, USA) was consisted of a Model 515 pump, a Model 710 plus autosampler and a Model 480 variable UV/Vis detector. A multi-channel Chrom and Spec software for chromatography (version 1.5×) was used for data processing. A dry air oven (Melag, Germany) and a Memmert water bath (Gmb+Co. KG, Germany) were used for heating. A 100 W tungsten lamp and a low

***Address for correspondence**
E-mail: souri@sina.tums.ac.ir

Accepted 30 May 2015
Revised 10 January 2015
Received 12 May 2014
Indian J Pharm Sci 2015;77(3):348-351