Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(19):14-18
(http://www.derpharmachemica.com/archive.html)

Analytical Description of 5-Nitroimidazole Derivative "Satranidazole"

Abhay Bhardwaj[1*], Jyoti Sharma[2], Daksh Bhatia[1], Anuj Pathak[1], Nagarajan K[1], Jagannath Sahoo[1]

[1]KIET School of Pharmacy, Ghaziabad-201206, Uttar Pradesh, India
[2]Jubilant Chemsys, Noida-201301, Uttar Pradesh, India

ABSTRACT

Satranidazole is a type of antiprotozoal drug which belongs to the nitroimidazole group. It is highly effective, well accepted and clinically useful against protozoa. It is two times more active than other nitroimidazoles against amoebiasis and giardiasis. It is more active against anaerobes than other nitrogen containing imidazoles. Although much research work has been carried out on satranidazole regarding pharmacological screening and formulation development but till now structural description of satranidazole is not summarized in single literature text. The present study discusses the melting point, UV-Visible, Proton Nuclear Magnetic Resonance (^{1}H-NMR), Mass, Fourier Transform Infra-Red (FTIR) data of satranidazole. Additional ^{13}C-NMR was used to provide the maximum analytical details of structure of satranidazole.

Keywords: Satranidazole, ^{1}H-NMR, ^{13}C-NMR, Mass, FTIR

INTRODUCTION

Satranidazole, chemically it is 1-methylsulphonyl-3-(1-methyl-5- nitro-2-imidazolyl)-2-imidazolidinone [1], is one of the large series of 5-nitroimidazoles with potent antiprotozoal activity against *Entamoeba histolytica*, *Trichomonas vaginalis* and *Giardia* [2]. Satranidazole is a yellowish, crystalline yellow powder and slightly hygroscopic in nature [3], insoluble in water and soluble in dioxane and Dimethyl Formamide (DMF). Satranidazole a new derivative of 5-nitroimidazole where second carbon of imidazole ring is linked with first nitrogen of imidazolidinone. The drug Satranidazole damages the DNA extensively and breakage of nucleic acid proceeds *via* strand breakage and helix destabilization [4]. It is commonly used in amoebic liver abscess, trichomoniasis and giardiasis with adverse effects like headaches, palpitations, high blood pressure, hot flushes, weakness, dizziness, nervousness, dry mouth, change in taste etc. The present study have goal to collect and ensure all the valuable analytical and spectrometric information's regarding satranidazole molecule.

MATERIALS AND METHODS

Materials and instruments

Satranidazole pure yellowish fine powder was procured from Alkem laboratories, Hyderabad (India). All other chemicals and reagents were of pure analytical grade and were used as supplied by CDH (New Delhi, India). Freshly prepared distilled water was used throughout the duration of study. Electronic Balance (AX200, Shimadzu), Melting point apparatus (Digimelt, MPA161, SRS, Made in USA), FTIR (IR Affinity-1, A213750, spectrophotometer, Shimadzu), ^{1}H-NMR spectrophotometer (Bruker, 400 MHz, Made in Switzerland), ^{13}C-NMR spectrophotometer, (Bruker, 400 MHz, Made in Switzerland), Mass spectrophotometer (Waters, Acquity-UPLC-SQ-Mass detector, made in US), UV spectrophotometer (UV 1800, Shimadzu) were used in this study.

Melting point determination

Load capillaries with satranidazole sample. Insert capillaries into the chassis holes near into the DigiMelt oven. Begin ramping the temperature at the ramp rate. Finally recorded the data during the course of melt. After completion of operation the melting point of satranidazole was found to be 189°C [5].

UV spectroscopic analysis

UV spectroscopic of satranidazole was acquired on a UV-1800, Shimadzu series spectrophotometer with 1 cm quartz cuvette [6-8]. The analysis was performed using wave length 200-400 nm. Stock solution had prepared in methanol of concentration 1 mg/ml and further dilutions occur up to 10 µg/ml. A λ_{max} was found to be 320 nm and absorbance was recorded as 0.423 (Figure 1).

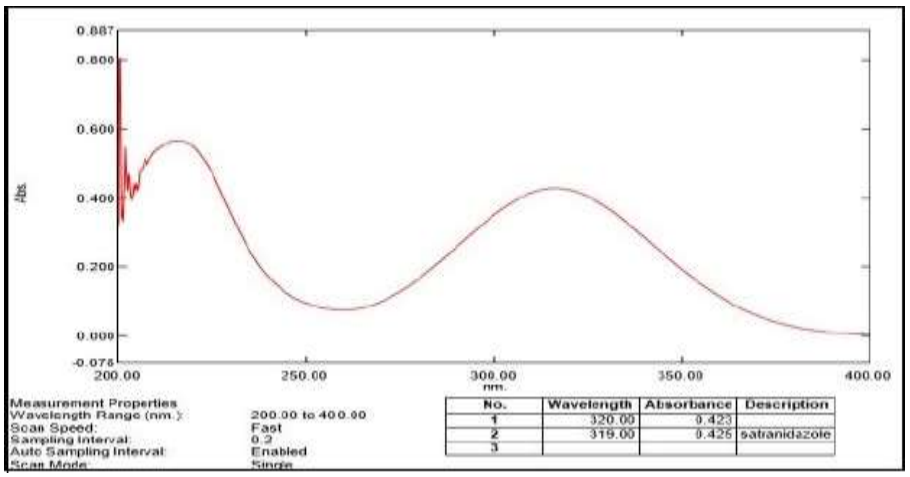

Figure 1: UV spectra of satranidazole

FTIR spectroscopic analysis

The FTIR of satranidazole was obtained using KBr discs. Each disc contained about a 2 mg sample and 250 mg of KBr. The spectra were recorded in the 4000-400 cm^{-1} range. Each sample was scanned 45 times with a resolution of 2 cm^{-1}. A spectrum of satranidazole was normalized (Figure 2). Functional groups present on the chemical structure of satranidazole give characteristic vibrational peak (Stretching, bending etc.,) on FTIR spectra, which is unique for that particular functional group. These vibrational peaks interpreted for structural characterization [9] of satranidazole were tabulated in Table 1.

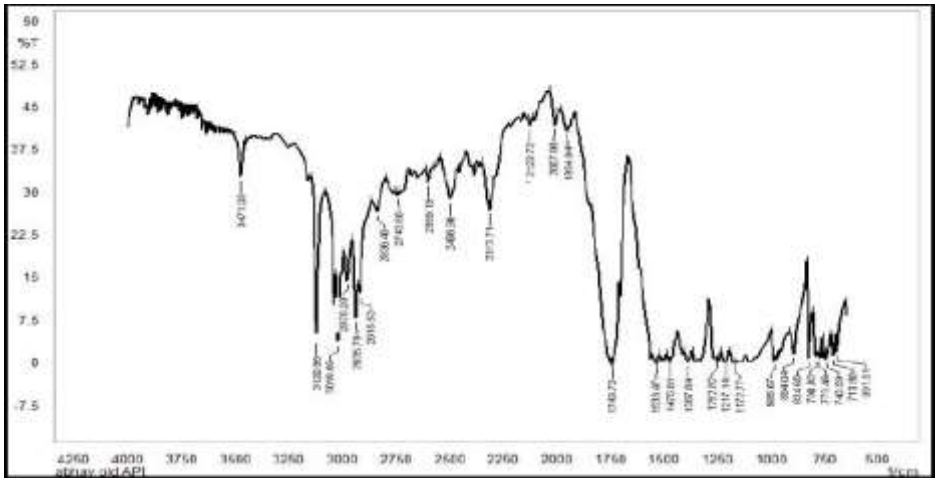

Figure 2: IR spectra of satranidazole

IR data interpretation of satranidazole [10,11]

Table 1: Interpretation of IR

S. No.	Wave number expected range (cm^{-1})	Wave number observed range (cm^{-1})	Characteristic functional group feasible	Compound type
1	3500-3400	3471.05	N → H stretching	(i) Five membered ring (ii) Hetero aromatics (imidazole)
2	3100	3120.96	C → H stretching	
3	770-710	743	C ↓ H δ opposite bend	
4	1690-1520	1743.72-1533.47	C=N stretching	
5	3090-2860	2935.78-2915.53	C → H stretching	Cyclic alkanes
6	2820-2780	2836.45	C → H stretching (CH_3-N)	Alkanes
7	3000-2840	2976.29	C → H stretching	
8	1470-1430	1475.61	C ↓ H δ bend assymetric	
9	1395-1365	1387.84	C ↓ H δ bend symmetric	
10	3095-3045	3019.68	C=H stretching	Alkenes
11	1005-675	24.60-691.51	C ↓ H δ oop bend	

12	1420-1250 (Dimer; very strong)	1387.84-1252.82	N=O stretching	Nitro compound
13	1560-1470 (Very strong)	1533.47-1475.4	NO_2 stretching symmetric	
14	1100	1100	C–N stretching	
15	1420-1000 (Very strong)	1387.84-1172.77	O=S=O	Sulfone
16	910-900	894.04	S-N stretching	
17	870-690	824.6	S-O stretching	
18	1775-1705 (Strong)	1743.72	C=O stretching	Cyclic ketone

^{1}H-NMR spectroscopic analysis

The proton nuclear magnetic resonance spectrum of a 4.6% (w/v) solution of satranidazole was obtained in deuterated Dimethyl Sulfoxide (DMSO-d_6) and is described in Figures 3 and 4. The band assignment were referenced relative to DMSO-d_6 (at 2.5 ppm), and the hydrogen atom assignment of satranidazole are following [12]: ^{1}H-NMR (400 MHz, δ ppm/DMSO): 8.12 (s, 1H), 4.02 (dd, J=8.0 Hz, 2H), 3.98 (dd, J=8.0 Hz, 2H), 3.75 (s, 3H), 3.37 (s, 3H).

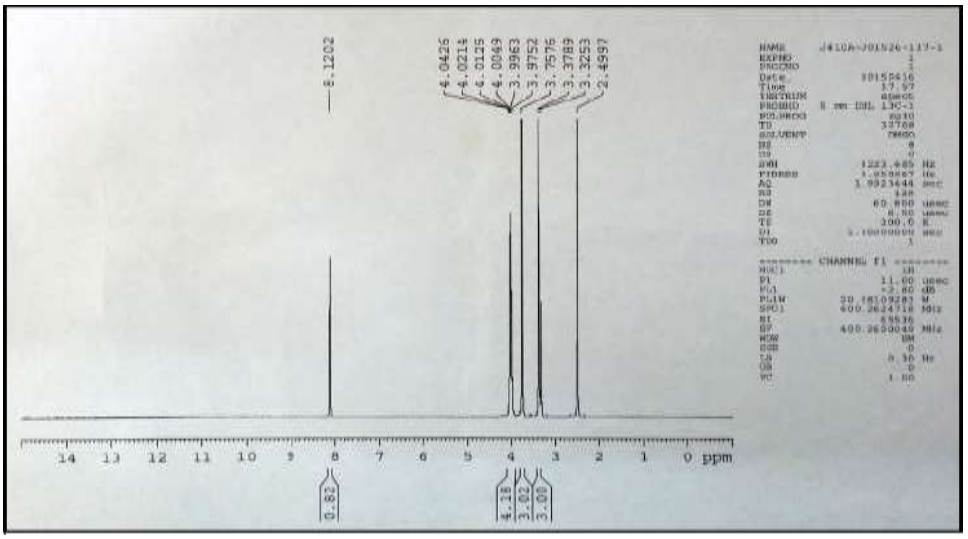

Figure 3: ^{1}H-NMR spectra of satranidazole

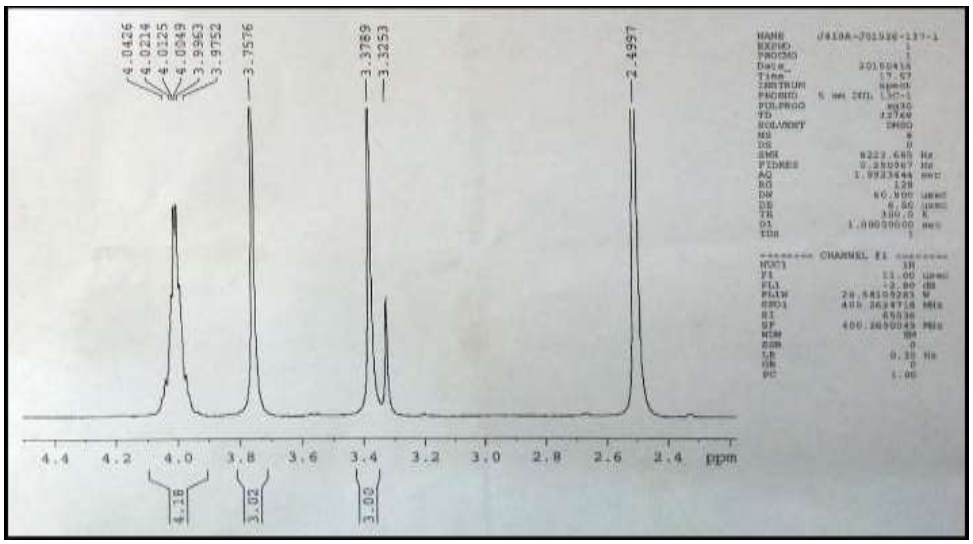

Figure 4: ^{1}H-NMR spectra of satranidazole

^{13}C-NMR spectroscopic analysis

^{13}C-NMR spectroscopy is generally done for the determination of number of carbon atom present in the unknown molecule (Figures 5-7). Determination of satranidazole is as follows [13,14]: ^{13}C-NMR (100 MHz, δ ppm/DMSO-d_6): 152.5 (C), 142.9 (C), 137.8 (C), 131.1 (CH), 43.0 (CH_2), 42.2 (CH_2), 38.9 (CH_3), 34.58 (CH_3).

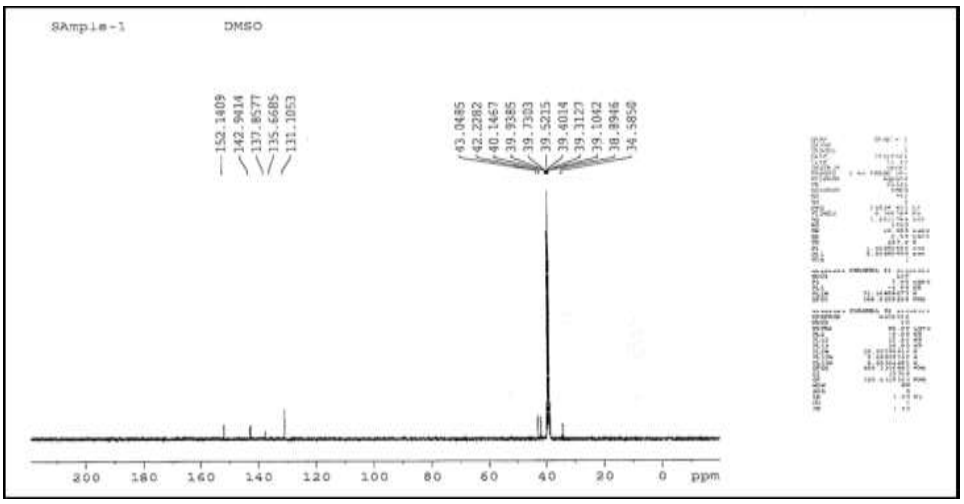

Figure 5: ^{13}C-NMR spectra of satranidazole

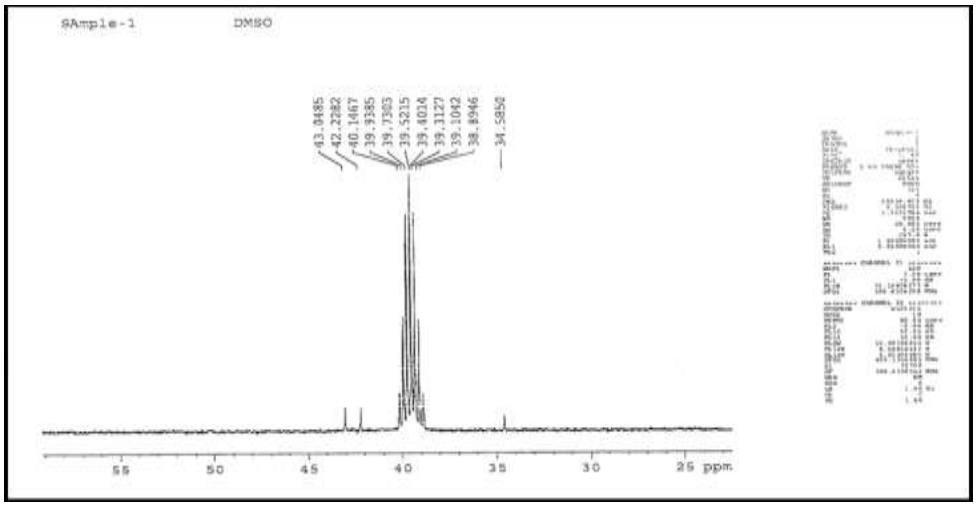

Figure 6: ^{13}C-NMR spectra of satranidazole

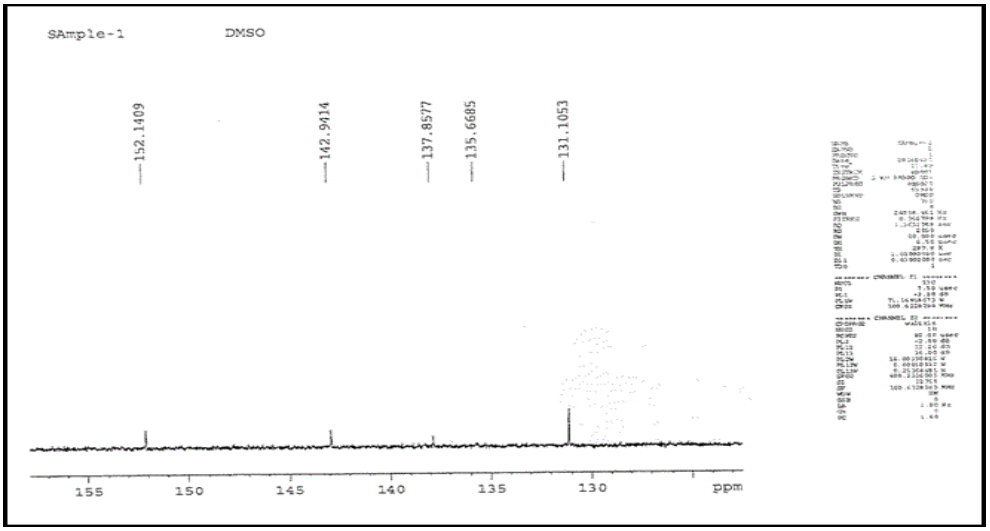

Figure 7: ^{13}C-NMR spectra of satranidazole

Mass spectroscopic analysis

A mass spectrum is determination of quantitative data of mass-to-charge ratios by way of mass spectrometry. A mass spectrum is obtained for satranidazole (Figure 8). The use of mass spectrometry to obtain chromatographic separation techniques such as liquid chromatography. The spectra are formatted as is known in the art having mass-to-charge values (i.e., m/z values) on an x-axis and quantitative values (e.g., intensity)

along a y-axis [15**]**. M as a pale yellow semi-solid (87 mg, 77%). R_f (Ethylacetate/Hexane: 1.5/3)=0.5. MS for $C_8H_{11}N_5O_5S$: calculated. $[M+H]^+$: 289.2684, found: 288.

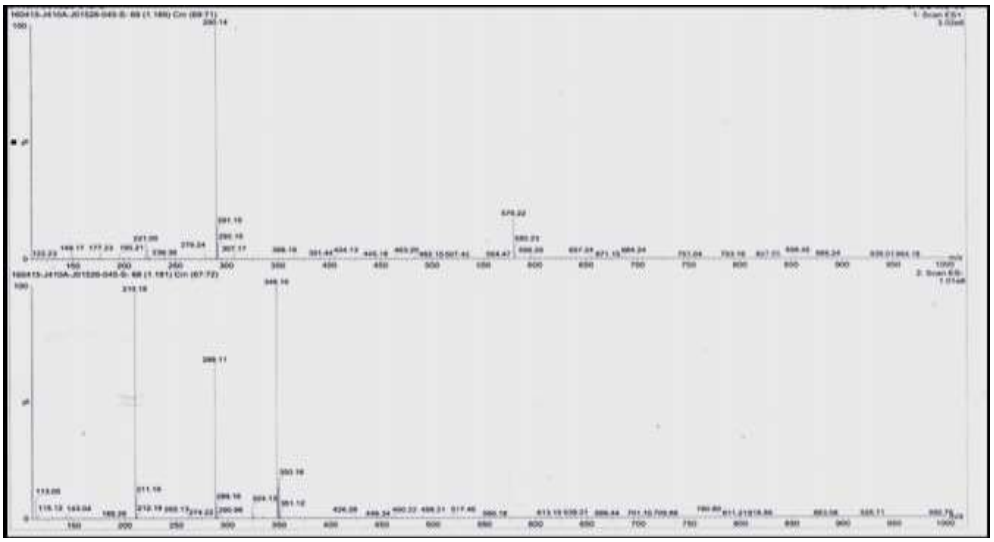

Figure 8: Mass spectra of satranidazole

RESULTS AND DISCUSSION

A sharp melting point of satranidazole was observed at 189°C, which indicates the authenticity and purity of sample. The UV spectra of satranidazole clearly show the λ_{max} at 320 nm, which specify the presence of satranidazole molecule. The I.R. spectra of the satranidazole produce various peaks of specific frequency (cm^{-1}), which almost resembles with functional groups and hetero-aromatic ring systems present in the structure of satranidazole. Observed wave number (cm^{-1}) like 3471.05, 3120.96, 743, 1743.72-1533.47, 2836.45, 3019.68, 1387.84-1252.82, 1533.47-1475.4, 1100, 1387.84-1172.77, 894.04, 824.60, 1743.72 clearly indicates the presence of N-H Str., C-H Str., CH δ opposite bend, C-H Str. (CH_3-N), C=H Str., C=N Str., N=O Str., NO_2 Str. sym., C^-N Str., -SO_2-, S-N Str., S-O Str. and ketone functionality.

^{1}H-NMR spectra clearly show the presence of total eleven hydrogen atoms exists on different location of satranidazole molecule. At δ ppm value 8.12, a singlet (s) peak has observed for 1H of imidazole ring, at δ ppm values 4.02 and 3.98 two doublet of doublets (dd) peaks have been observed for 4H of imidazolidinone ring and δ ppm values at 3.75 and 3.37 indicates singlets for total 6H of two methyl groups respectively. ^{13}C-NMR spectra specify existence of eight carbon atom in the skeleton of satranidazole. The different δ ppm values for corresponding carbon atoms were found as 152.5 (C), 142.9 (C), 137.8 (C), 131.1 (CH), 43.0 (CH_2), 42.2 (CH_2), 38.9 (CH_3), 34.58 (CH_3). In Mass spectra of satranidazole a molecular ion peak i.e., $[M+H]^+$value was calculated as 289.26 and observed m/z value is 288.11 (approx. 289.26). So the calculated value is almost similar to the observed m/z value.

CONCLUSION

Although the molecule in light has been described analytically through several studies but this study aimed at providing the upcoming researchers the complete analytical profile of satranidazole along with the available spectra. We have explored satranidazole under melting point determination, UV-Visible spectrophotometry, IR spectroscopy, ^{13}C-NMR spectroscopy, ^{1}H-NMR spectroscopy and mass spectroscopy.

ACKNOWLEDGEMENTS

The authors would like to acknowledge to the KIET School of Pharmacy, Ghaziabad for providing the instrumental facility. We are also grateful to Mr. Himanshu Aggarwal, Assistant Professor KIET School of Pharmacy, who has supported and helped in this research work. We are also thankful to our Director, Dr. J. Girish and CAO, Dr. Manoj Goel, KIET Group of Institutions for providing all the facilities.

REFERENCES

[1] http://sci-toys.com/scichem/jqp016/41841.html.
[2] B.H. Mruthyunjayaswamy, S.M. Patil, S.A. Raju, *Indian. J. Pharm. Sci*., **2001**, 63, 433-436.
[3] https://en.wikipedia.org/wiki/Electronic_journal.
[4] A. Zahoor, R.C. Knight, P. Whitty, D.I. Edwards, *J. Antimicrob. Chemother*., **1986**, 18(1), 17-25.
[5] Operation and Service Manual MPA160 and MPA161 DigiMelt Student Melting Point System Revision 1.9, **2009**.
[6] P.D. Panzade, K.R. Mahadlik, *East. Pharm.*, **2000**, 43, 115.
[7] P. Nagaraja, K.R. Sunitha, R.A. Vasantha, H.S. Yathirajan, *J. Pharm. Biomed. Anal*., **2002**, 28, 527.
[8] T. Saffaj, A. Charrouf, Y. Abourriche, A. Abboud, M.B. Bennamara, *Formaco.*, **2004**, 59, 843.
[9] L.G.M. Maria, M. Paola, M.R. Antonio, *Eur. J. Pharm. Sci*., **2003**, 20(1), 125-131.
[10] A. Arunachalam, P. Sudhakar, *IJRPNS*., **2012**, 1(1), 1-10.
[11] N. Huyghebaert, A. Vermeire, J.P. Remon, *Int. J. Pharm.*, **2005**, 298, 26-37.
[12] H. Allars, M.D. Coleman, R.S. Norton, *Eur. J. Drug. Metab. Pharmacok.*, **1985**, 10(3), 253-260.
[13] R.G. Shulman, T.R Brown, K. Ugurbil, S. Ogawa, *Science.*, **1979**, 205, 160-166.
[14] R.S. Norton, *Bull. Magn. Reson*., **1980**, 3, 29-48.
[15] L.F. Capitan-Vallvey, A. Ariza, R. Checa, N. Navas, *J. Chromatogr. A.*, **2002**, 978, 243-248.