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New Fluorimetric Method of Determination for Lisinopril Dosage Forms

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ABSTRACT
New fluorimetric analytical method which is simple, accurate, precise, specific is developed for determination of Lisinopril. The fluorimetric determination of Lisinopril is based on the formation of complex between Lisinopril and Fluorescien, measured at excitation wavelength of 366 nm and emission wavelength of 475 nm. Linearity was observed in the range of 0.03 – 0.15 µg ml^{-1}. The fluorimetric method shows regression coefficient of 0.99971, and Relative Standard Deviation 0.527. Tablet dosage forms were estimated were complied with percentage recovery studies of 99-100 %. The method was validated for linearity, precision, accuracy, specificity and statistically expressed.

Keywords: Lisinopril, Fluorescien, Coupling reaction, Fluorimetry.

INTRODUCTION

Lisinopril is ACE inhibitor which is used as antihypertensive and in the treatment of cataract. [1] The official analytical methods for Lisinopril described are potentiometric titration and HPLC [2-4], various spectrophotometric methods [5-18], chromatographic methods of analysis such as micellar electrokinetic chromatography and gas liquid chromatography [19-20], Capillary electrophoresis, fluoroimmunoassay, radioimmunoassay and fluoroenzymatic assay have also been reported. [21-22] The estimation with ninhydrin reported in sodium hydroxide and sodium carbonate associated with interference of concentrated blank solution in absorption and is time consuming. The available methods are associated with drawbacks such as low reliability due to isomerisation, less sensitive, measurement at lower wavelength, pH dependent, inaccessibility and requirement of expertise.

So there is need to develop new simple, accurate, precise, specific analytical method which sensitive and is easily accessible. The present study aimed to develop fluorimetric method to determine the Lisinopril in pure form or in formulation. Fluorimetric method is based upon the condensation reaction between primary amino group of Lisinopril and Fluorescien to form fluorescent derivative (LSFN) in methanol at 60°C for 5 min (Fig. 4).

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The formation of fluorescent derivative was confirmed by the UV (λmax 227 nm), NMR, Mass and IR spectra (Fig. 5-10). Relative fluorescent intensity was measured with excitation filter of 366 nm and emission filter of 475 nm setting the fluoremeter to 100% intensity with concentration of 0.1µg/ml standard solution using methanol as blank. The reagent fluorescien shows 0.00009 µg ml^{-1} as maximum of limit of measurable concentration whereas fluorescent derivative (LSFN) limit is beyond the range of reagent (0.03 - 0.19 µg ml^{-1}). Under the limit of measurement, fluorescent intensity is proportional to the concentration of analyte. The stability of reaction mixture was determined. The developed method was validated for parameters as per the ICH guidelines.

MATERIALS AND METHODS

Elico Fluorimeter, model CL-53 was used for fluorimetric determination. The fluorescence intensity of test and reference solutions was recorded in 3 ml borosilicate cells. The Relative Intensity was measured with filters of excitation wavelength of 366 nm and emission wavelength of 475 nm.

Standard drug, marketed formulations and reagents used

The experimentation Lisinopril dihydrate standard drug was procured from Unimark Pharmaceuticals Ltd, Vapi, Gujarat, India, and certified to contain 99.3%. All the chemicals, solvents and reagents used in the study were of analytical grade. Listril 5 mg manufactured by Torrent Pharmacueticals Ltd, Lipril 10 mg manufactured by Lupin Ltd and Lisoril 5 mg manufactured by Ipca Laboratories Ltd were three commercial tablets of Lisinopril used for sample estimation.

Fluorimetric Method

Lisinopril of 100 mg was transferred to 100 ml volumetric flask. Add 50 ml of methanol, shake well to dissolve, and then Fluorescien of 0.07526 mg was added. The mixture was shaken and heated at 60°C for 5 min, cooled, and then final volume was made with methanol. Various volumes were transferred to 50 ml volumetric flaks so as to produce the different concentrations in the range of 0.03 µg-0.15 µg. Standard Lisinopril solution of 0.1µg/ml was used to set 100% intensity using methanol as blank.

Procedure for fluorimetric estimation of commercial tablets

Weigh accurately 20 tablets and crushed to fine powder. The tablet powder equivalent to 100 mg was weighed and added to 40 ml of methanol. The mixture was stirred well filtered; the filtrate was transferred to 100 ml of volumetric flask. Fluorescien of 0.07526 mg was weighed accurately and dissolved in 50 ml of methanol and then transfer this solution to the Lisinopril solution. Mixture was heated at 60°C for 5 min, cooled to room temperature and then final volume was made with methanol. Standard Lisinopril solution of 0.1µg/ml was used to set 100% intensity using methanol as blank. The relative intensities of other sample dilutions were recorded using methanol as blank solution.

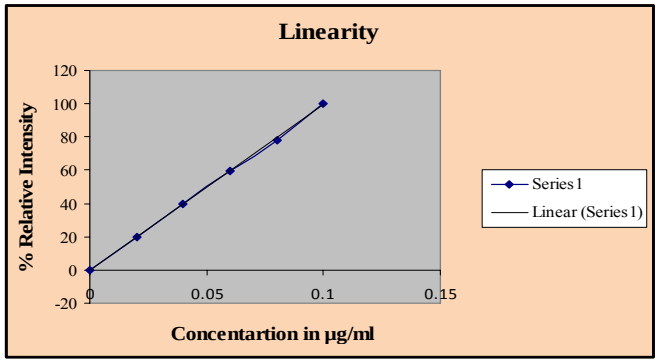

Fig. 1: Linear relationship between % Relative intensities and Concentration

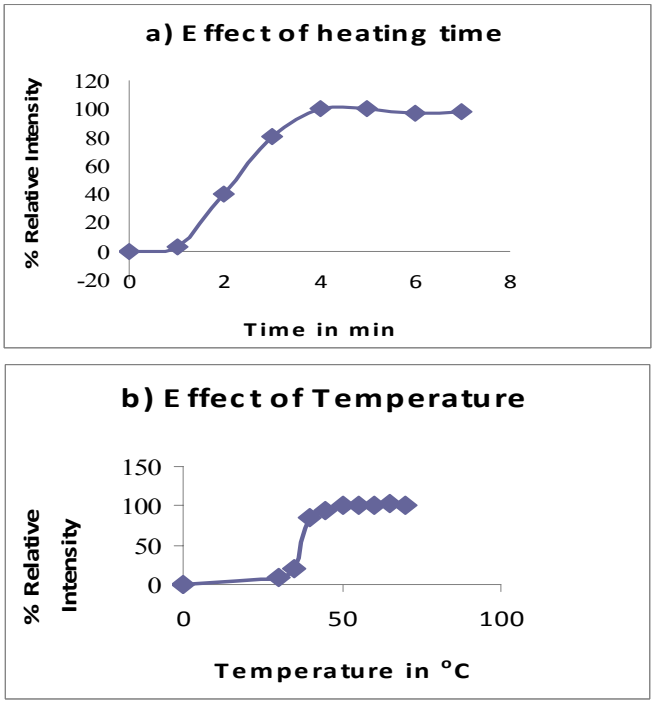

Fig. 2: Graphical representation of effect of (a) heating time and (b) temperature on % Relative Intensity in Fluorimetric determination

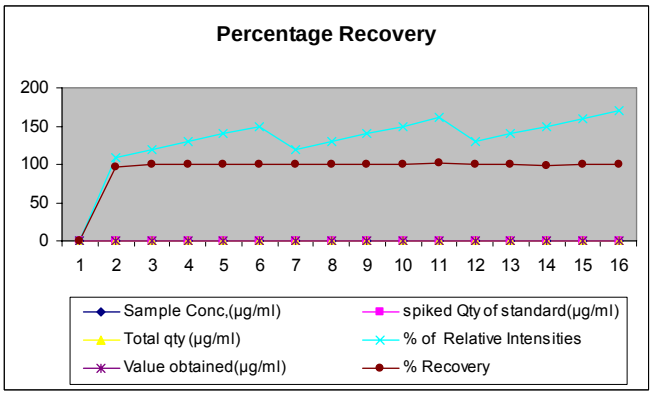

Fig. 3: Fluorimetric determination: Graphical representation of % Recovery studies with constant quantity of sample and spiked quantity of drug

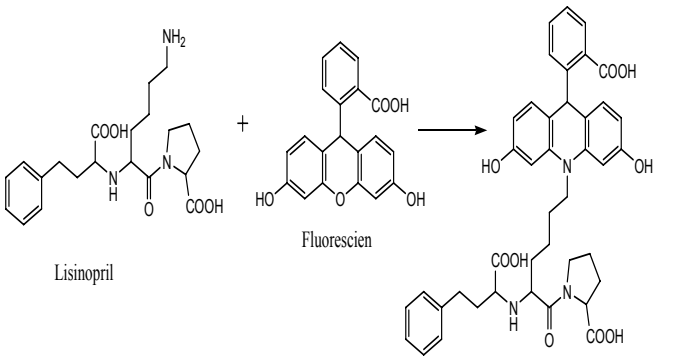

Fig. 4: Proposed reaction mechanism for the formation of fluorescent derivative of Lisinopril with Fluorescien

Table 1 : Statistical calculation of validation parameters

S. No	Parameter	Statistical Value
1.	Standard Deviation	0.03162
2.	Relative Standard Deviation	0.52704628
3.	Coefficient of Variation	52.7046283
4.	ANOVA	36.30868
5.	Correlation Coefficient	0.99971
6.	Lower limit of Detection	0.0001049 µg/ml
7.	Lower limit of Quantification	0.000318 µg/ml
8.	Slope	994.06536
9.	Intercept	0.083576
10.	% Recovery	99-100 %

a. Equation of linearity is Absorbance or Relative Intensity = Slope × Concentration + Intercept.

RESULTS AND DISCUSSION

The developed fluorimetric method makes use of simple reagent, shows linearity range of 0.03µg to 0.15 µg (Fig. 1), producing the data at appreciable sensitivity even in low concentration. Fluorimetric determination is optimized for the factors affecting the coupling reaction (Fig. 2). Statistical analysis of experiment shows the accuracy of 99-100 % (Fig. 3), relative standard deviation was 0.527 and coefficient of correlation was 0.99971.Samples of marketed formulation was estimated. The method was validated for analytical parameters like accuracy, Linearity, precision, specificity, Limit of Detection and Limit of quantification and statistically expressed were found to be within the standard specification (Table 1). Hence developed method simple, accurate, specific and precise which can applied in quality control for the estimatiom of lisinopril.

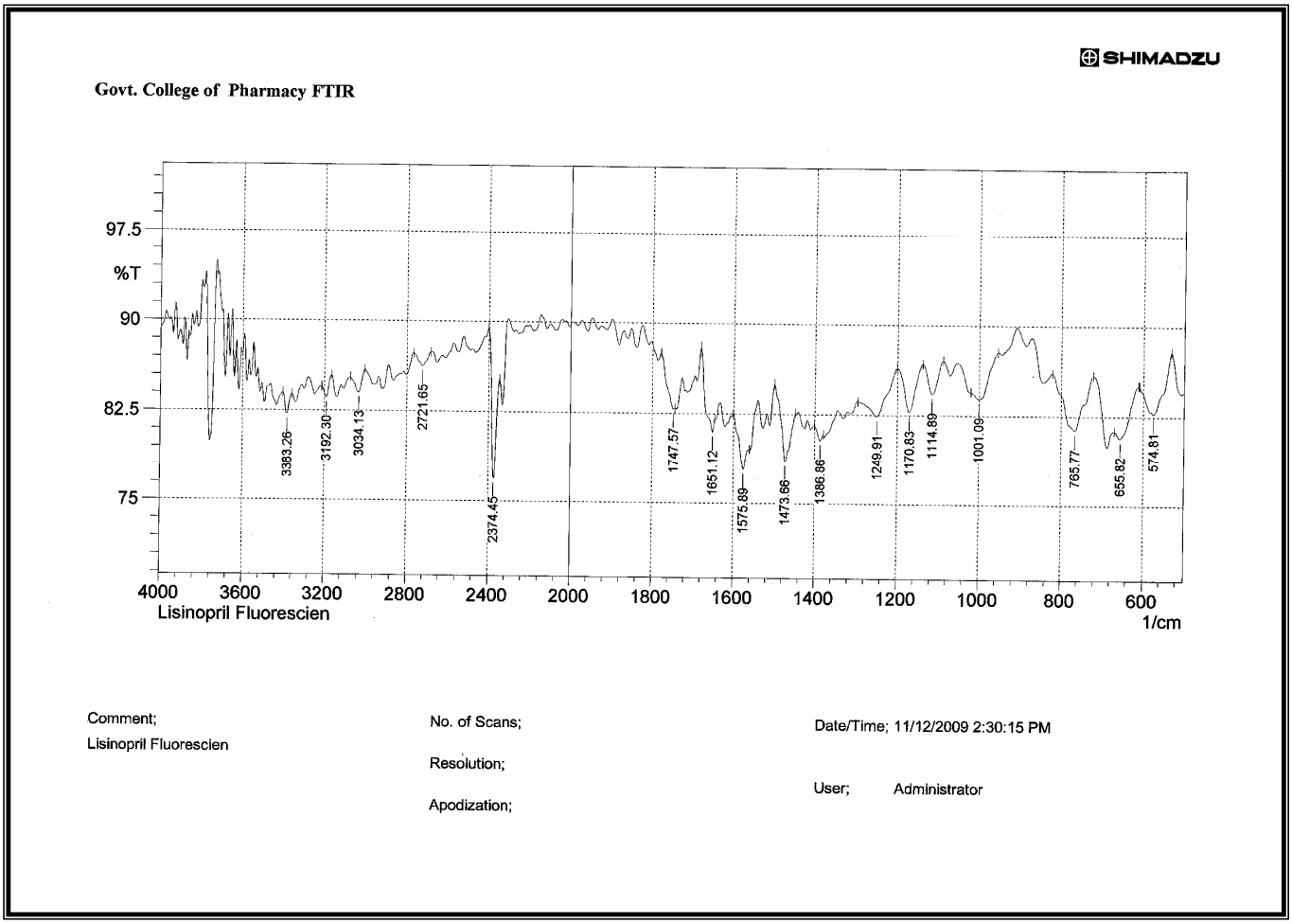

Fig. 5: IR Spectrum of fluorescent derivative

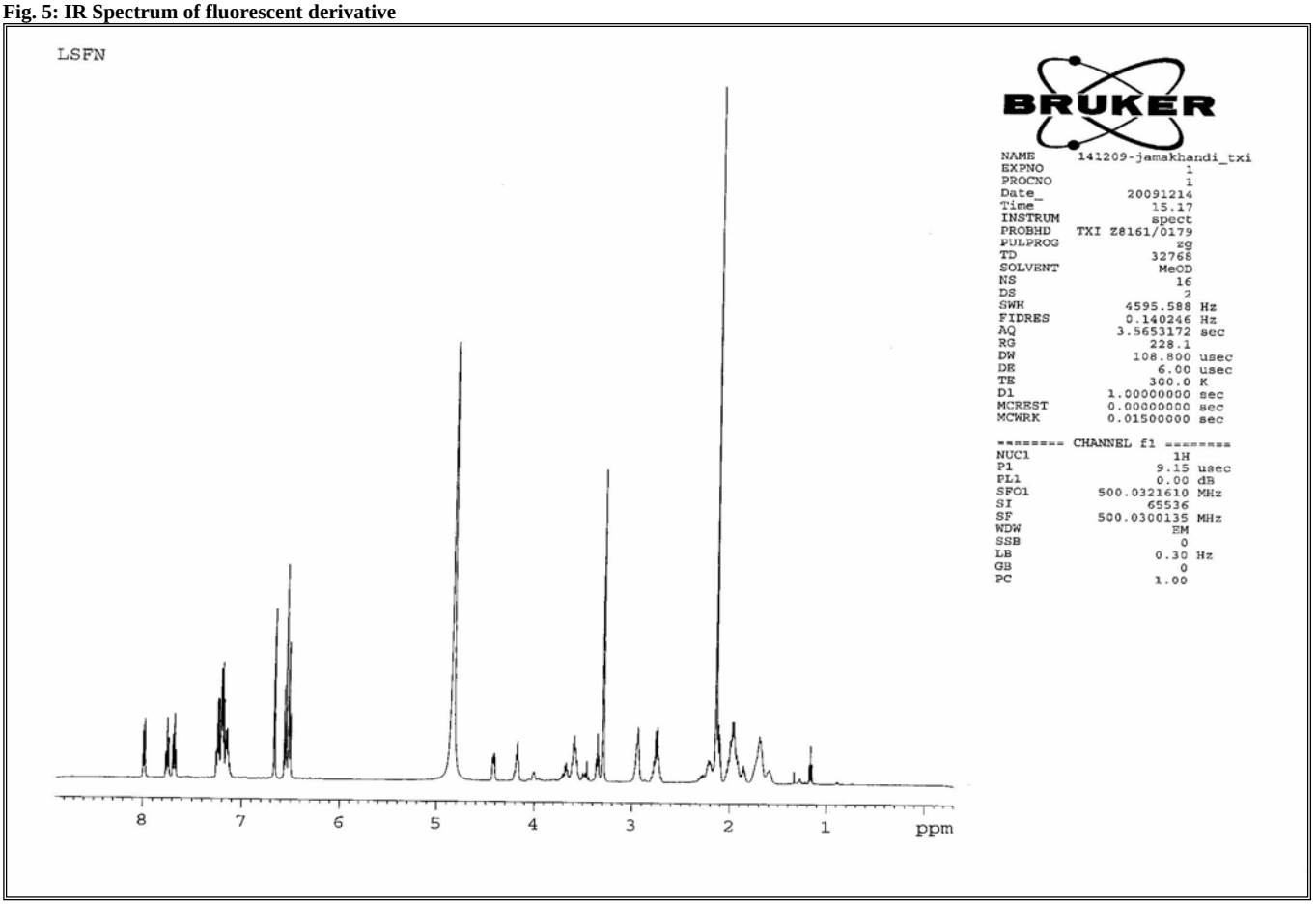

Fig. 6: NMR Spectrum of fluorescent derivative

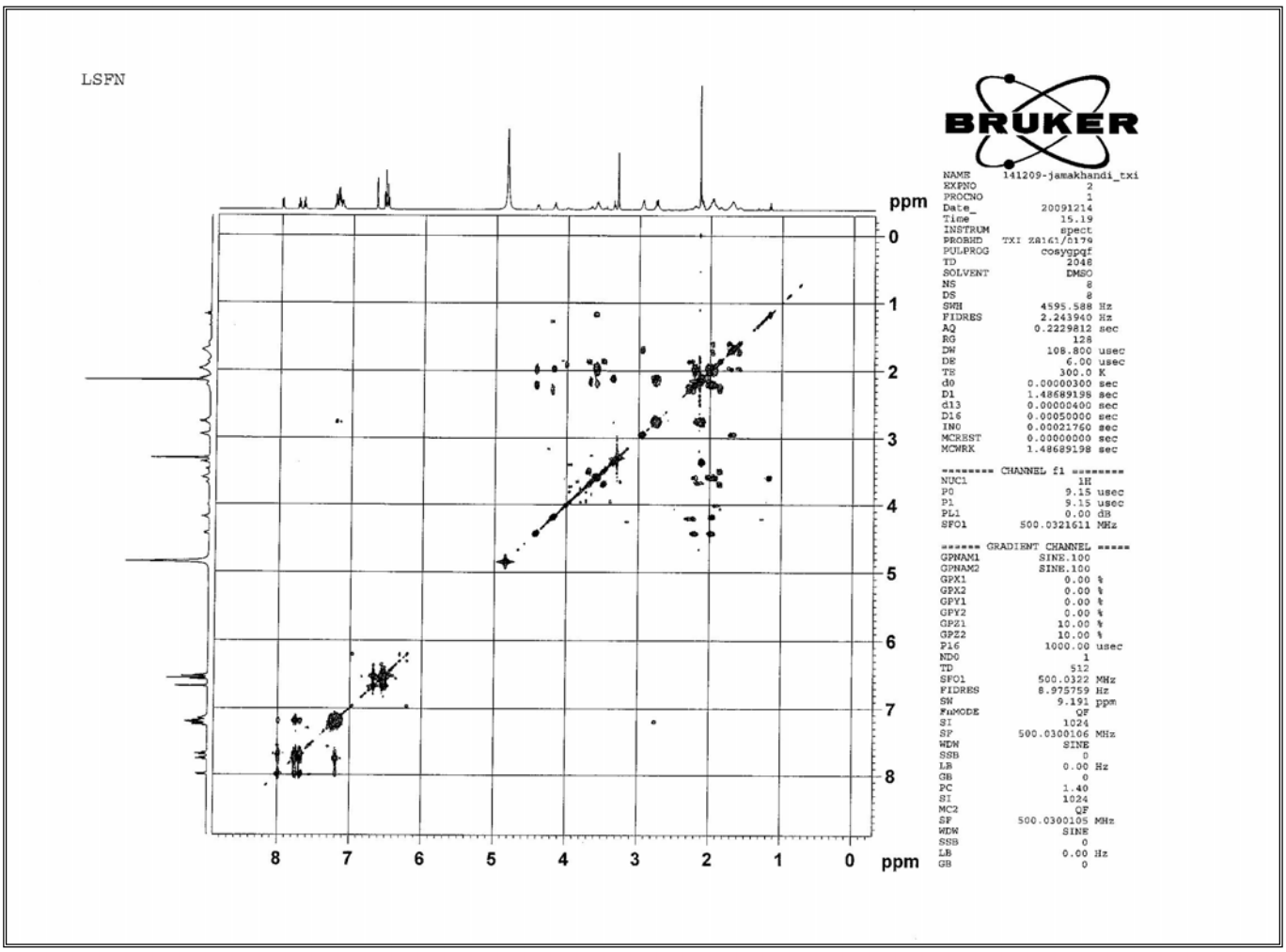

Fig. 7: 2D HNMR Spectrum of fluorescent derivative

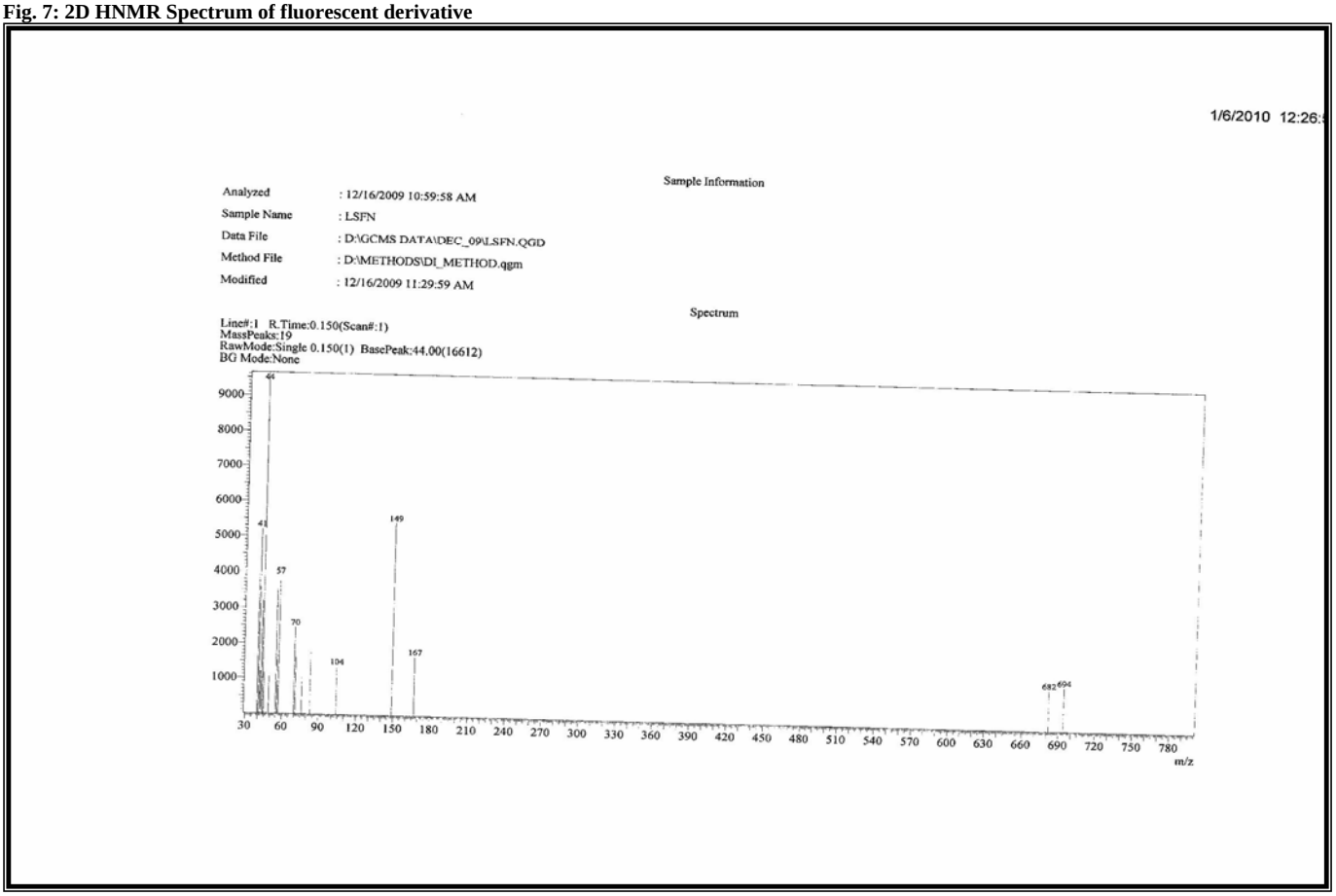

Fig. 8: Mass Spectrum-1of fluorescent derivative

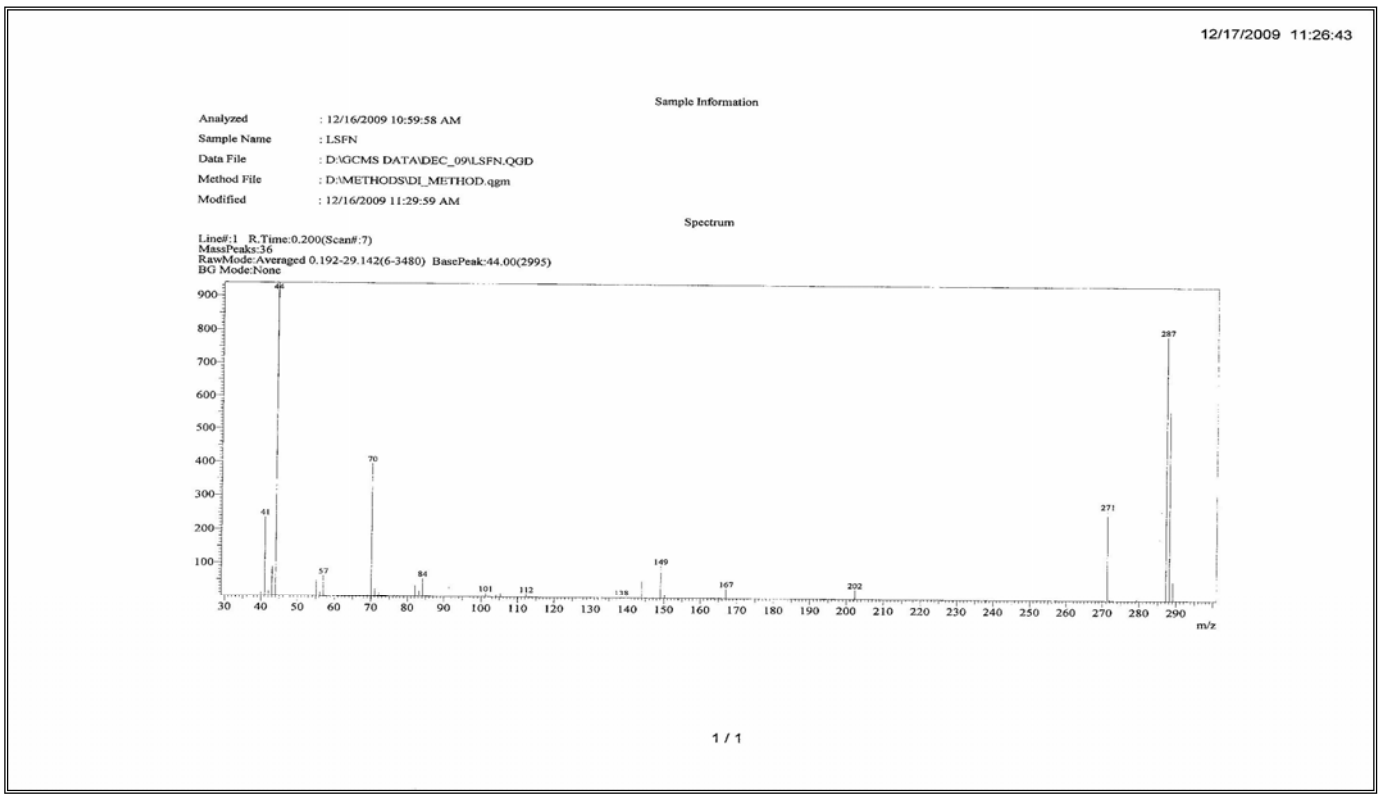

Fig. 9: Mass Spectrum-2 of fluorescent derivative

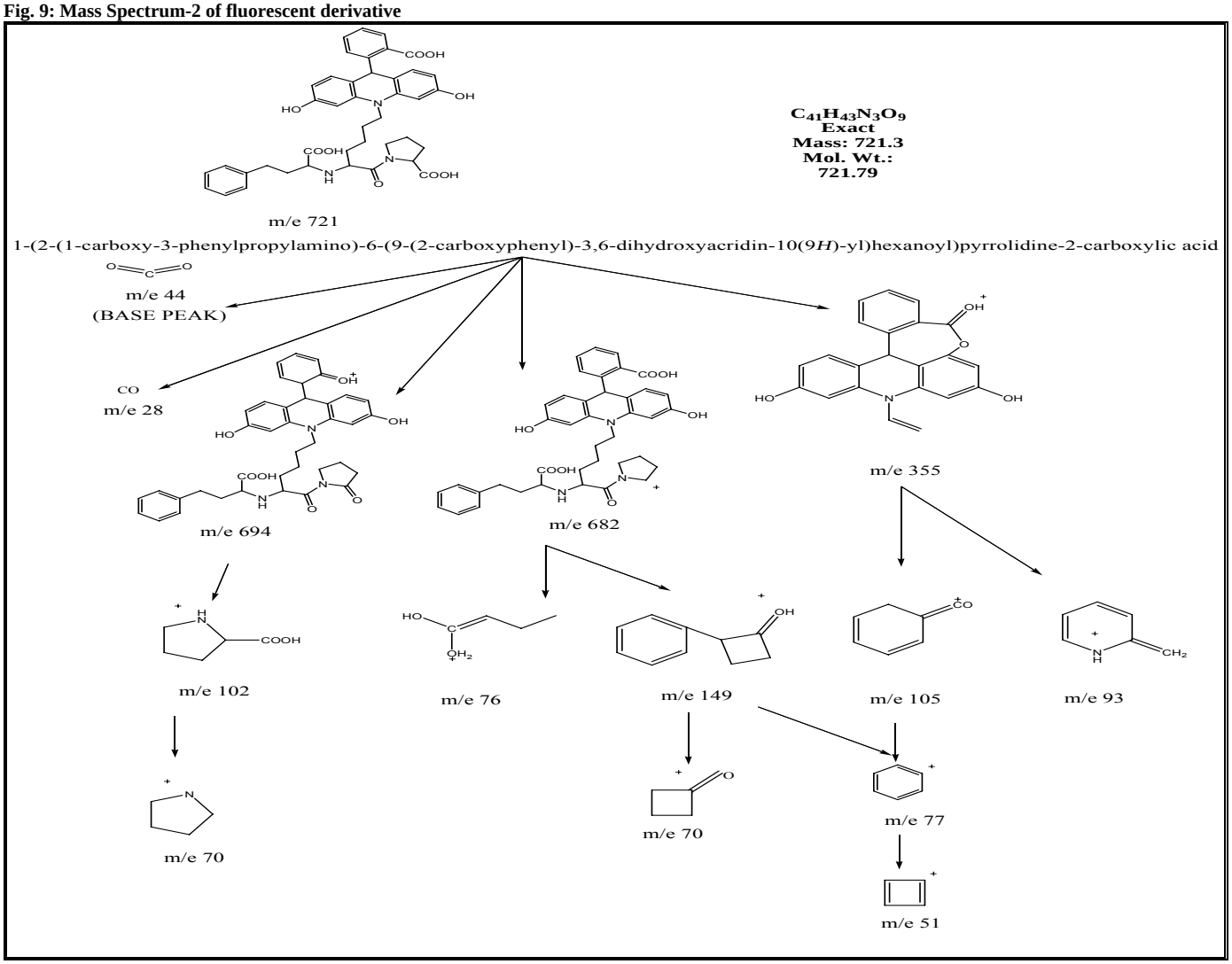

Fig. 10: Fragmentation pattern of LSFN in Mass spectra

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