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Derivative Spectrophotometric Determination of Adapalene in its Bulk and Pharmaceutical Dosage Form

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A rapid, simple UV spectrophtometric method is developed for routine analysis of adapalene in quality control laboratory. Both bulk drug and pharmaceutical dosage form is validated by this method. From the solubility profile study, a specific solvent was selected methanol and acetonitrile (8:2), wavelength maxima of the drug was found to be 230.8 nm. Simultaneously a derivative spectrophotometric method was developed and validated. The λ_{max} and λ_{min} was recorded 236.8 and 222.7 nm respectively. In the proposed method, adapalene follows linearity in the concentration range 3-23 µg/mL with a correlation coefficient 0.9996. The method was validated statistically as per ICH guidelines and by recovery study. The standard deviation was 0.02431 and RSD was found to be 2.52 %, which is equivalent 2 % with excellence precision and accuracy.

Key Words: Derivative spectrophotometry, Determination, Adapalene.

INTRODUCTION

Adapalene (Fig. 1) is yellowish white powder, a naphthoic acid derivatives with retinoid-like properties bearing chemical name 6-[3-(1-adamantyl)-4-methoxy-phenyl] naphthalene-2-carboxylic acid. Its molecular formula is $C_{28}H_{28}O_3$ with molecular weight 412.52 g/mol. Adapalene is a third-generation topical retinoid primarily exhibits some retinoic acid-like activity but it reduces important features of the pathology of acne vulgaris by normalizing the differentiation of follicular epithelial cells. Its mechanism is similar to the mechanism of retinoic acid. Unlike retinoic acid, adapalene selectively binds to some nuclear retinoic acid receptors (RARs) and it is hypothesized that by selectively binding to certain nuclear retinoic acid receptors and not others[2,3]. The literature surveyed revealed that there are different type of analytical method like RP-HPLC, UV spectroscopy, NMR, FTIR[4], colourimetric method developed using plasma, therefore it is needed to develop the following method which is very simple, economical, precise, accurate, rapid and selective by UV derivative spectroscopy.

Adapalene pure drug was used for the development of analytical method, which was gifted by Sun Pharma, Baroda, India. Methanol and acetonitrile (8:2) was used as solublizing agent of AR grade (Merck), India for analytical purpose.

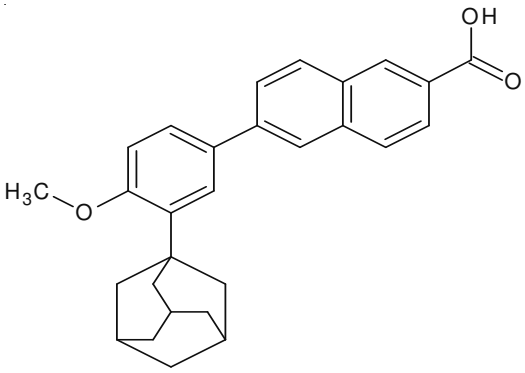

Fig. 1 Structure of adapalene

EXPERIMENTAL

Derivative spectroscopy was developed using zero crossing first derivative methodology. The derivative UV spectra for test and standard solutions were recorded in 1 cm quartz cells using JASCO V-630 double beam UV/VIS Spectrophotometer. The zero order and first derivative absorption spectra were recorded over a wavelength range of 200-400 nm against solvent blank. Acculab ACL-2104 (Stereos group) electronic balance was used for weighing the samples and class A volumetric glassware were used.

Spectrophotometeric condition: JASCO V-630 double beam UV/VIS spectrophotometer was used for the spectrophotomeric method development. Solvents play a vital role in UV spectroscopic method development, so taking different solvents or ratio of solvent finally methanol: acetonitrile was selected in the ratio of 8: 2 as solvent system. The λ_{max} was found for the pure drug solution at 230.8 nm and further process for derivative spectroscopy method was carried out.

Preparation of stock solution: Standard stock solution of adapalene was prepared by dissolving 20 mg of powdered drug in 20 mL of methanol: acetonitrile (8:2) in a volumetric flask to get a concentration of 1000 µgm/mL.

Preparation of workinig standard solution: The prepared stock solution was further diluted with methanol: acetonitrile (8:2) mL to get a concentration of 100 µgm/mL. Different aliquots of drug solution was prepared and transferred separately into a series of 10 mL volumetric flask and diluted upto 10 mL with the solvent ratio. Then the absorbances were measured at λ_{max} 230.8 nm against blank. A calibration graph of adapalene was plotted taking concentration on X-axis and absorbance on Y-axis (Fig. 2).

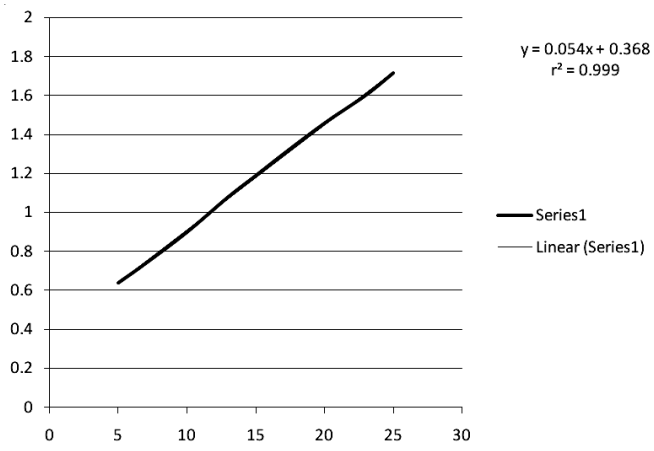

Fig. 2. Calibration curve for adapalene

Derivative spectroscopy[5-7]: The sample solution of adapalene drug was scanned and the zero order spectrophotometric curve was seen in UV spectroscopy at 230.8 nm and then the first order derivative spectrophotometric curve was seen in UV spectroscopy finally λ_{max} and λ_{min} was found to be at 236.8 and 222.7 nm, respectively (Fig. 3) and the sample solution was quantified within the concentration range 5 to 50 µg/mL to obtain a linearity of Beer's law limit from 7 to 25 µg/mL with a regression of 0.999.

Estimation of adapalene in its pharmaceutical dosage form (gel): Marketed formulation (gel) of adapalene was collected and extracted with sufficient amount methanol. A 10 mg equivalent weight of the formulation was mixed with 10 mL methanol. It was sonicated and then filtered with membrane filter (pore size 0.45 µm). Then suitable aliquots from the filtrate were taken further diluted with the solvent mixture to get the concentrations within the linearity range of standard curve. The absorbance of the prepared solutions was measured at 230.8 nm against a blank. The drug content of adapalene in the gel formulation was estimated using the regression line equation (y = mx + c).

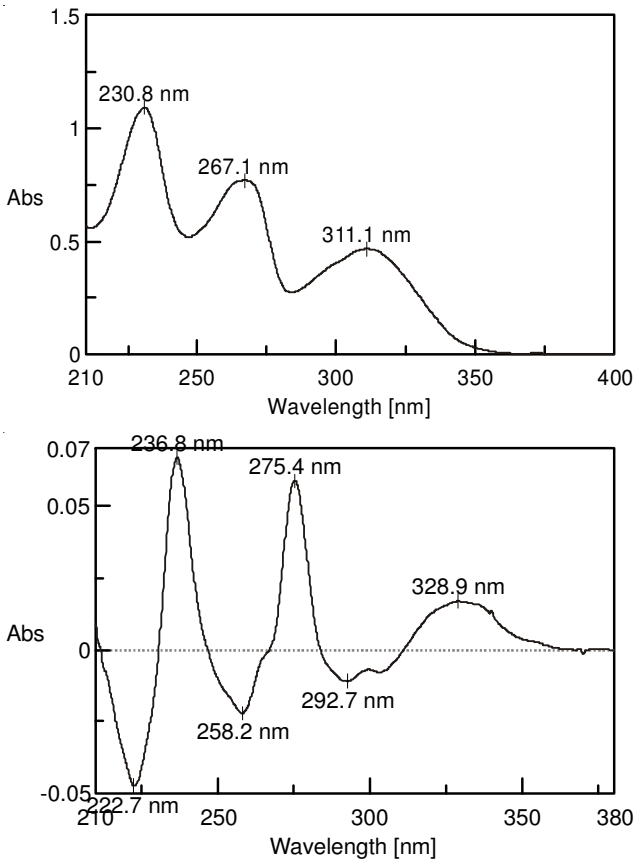

Fig. 3. Zero Order Spectra And First Derivative Spectra

RESULTS AND DISCUSSION

The proposed derivative spectroscopic method was carried out by using methanol: acetonitrile in the ratio of 8:2 as solvent system for adapalene and the λ_{max} was found in UV spectroscopy was at 230.8 nm and after first order derivatization the λ_{max} and λ_{min} was found to be 236.8 nm and 222.7 nm, respectively.

The stock solution was further diluted with the solvent ratio of methanol:acetonitrile (8:2) mL to get concentration of 100 µg/mL then different aliquots of drug solution was prepared and transferred separately in to 10 mL volumetric flask and diluted up to 10 mL with that same solvent ratio that is methanol:acetonitrile (8:2) mL then the absorbance was measured at λ_{max} 230.8 nm, which obeys Beer-Lamberts law. The regression equation was y = 0.054x + 0.368 where the correlation co-efficient was 0.999. The method was found to be precise when the sample solution was carried out for intraday and inter-day validation. By taking five replicates the intraday precision coefficient of variation was found to be 2.298 and inter-day precision coefficient of variation was found to be 1.7627. By taking these values confirm the intraday and inter-day precision of this method, which is shown in the Table-1.

The method was carried out by taking different formulations of pure drug adapalene, which was assayed and finally the amount was found to be in the range of 99.73 ± 0.98 to 102.8 ± 0.95 %, which is within the acceptable limit and that is shown in Table-2.

TABLE-3
RECOVERY STUDY OF ADAPALENE

Sample ID (%)	Concentration (µgm/mL)		Theoretical Content (µgm/mL)	Recovery of pure drug (%)	Stastical analysis
	Pure drug	Formulation			
S1-80	8	10	9	99.17	Mean = 99.78
S2-80	8	10	9	99.53	SD = 0.7718
S3 –80	8	10	9	100.65	% RSD = 0.7735
S1-100	10	10	10	99.81	Mean = 99.87
S2-100	10	10	10	99.65	SD = 1.3140
S3-100	10	10	10	100.15	% RSD = 1.3157
S1-120	12	10	11	99.73	Mean = 100.253
S2-120	12	10	11	100.17	SD = 0.6190
S3-120	12	10	11	100.86	% RSD = 0.6175

TABLE-1
PRECISION OF THE PROPOSED METHOD

Concentration of adapalene (µg/mL)	Observed concentration of adapalene (µg/mL)			
	Intra- day		Inter-day	
	Mean (n = 5)	Coefficient of variation (%)	Mean (n = 5)	Coefficient of variation (%)
15	1.8093	0.7224	1.2907	0.9587
20	2.0988	0.4643	1.9053	1.8379
25	2.9859	2.5958	2.0921	2.7925

TABLE-2
ASSAY DATA OF GEL FORMULATION

Brand name of the adapalene gel	Lable claimed	Amount found, mean (± SD)	% Amount found (± SD)
ADIFF	0.1 %w/w (15 mg)	15.43 ± 0.92	102.8 ± 0.95
ACLENE GEL	0.1 %w/w (15 mg)	14.96 ± 0.97	99.73 ± 0.98

The recovery studies were carried out by adding different amount of 80, 100 and 120 % of bulk sample of adapalene with the formulation 10 µgm/mL the RSD was found to be 0.902 %, which is shown in the Table-3. The proposed method obeys the linearity between concentration ranges of 5 to 30 µg/mL by taking 5 replicates of the analyte.

The specificity and selectivity of this proposed method was evaluated with regard to interference due to presence of any other impurities. The lowest concentration of the analyte was detected and the result was found out to be 4.854 and the lowest quantity of analyte was detected and the result was found out to be 16.181 for adapalene.

The robustness can be partly assured by good system suitability selection. The optimum UV spectroscopy condition set for this method have been slightly modified for sample adapalene dissolved in the drug matrix as a means to evaluate the method ruggedness.

Lastly the requirements for the system suitability are usually developed after method development and validation.

Conclusion

The validation of the method to determine adapalene in its bulk and pharmaceutical dosage form by first derivative spectrophotometry is an important contribution since earlier literature and pharmacoepia has not reported about it. The achieved results also confirmed that first derivative using peak-zero method could be used to analyze adapalene in its gel formulation. Further the proposed method is reliable, rapid and moreover inexpensive.

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