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SIMULTANEOUS ESTIMATION OF DAPSONE AND ADAPALENE IN GEL FORMULATION BY UV- SPECTROSCOPY

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Keywords:

Dapsone, Adapalene, UV- Visible Spectrophotometric method, validation

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ABSTRACT: Objective: A new, simple, sensitive, and economical UV spectrophotometric method was developed for the simultaneous analysis of Adapalene and Dapsone in pharmaceutical formulation. **Method:** This UV method was developed with Tetrahydrofuran and Distilled water as solvents. The wavelengths selected for analysis in the present method were 237 nm and 293 nm. The method was validated as per ICH guidelines. **Results:** The method was validated for linearity, accuracy, precision, specificity and robustness. Linearity was found to be within the concentration range of 0.05-0.25 µg/ml for Adapalene and 2.5-12.5 µg/ml for Dapsone. Accuracy for the method was determined by recovery studies. The % drug recovered was found to be 99-102% w/w. The % RSD values of repeatability and intermediate precision were found to be less than 2, providing method was precise in nature. From all these studies it was observed that there was no interference of excipients from the formulation during the analysis. **Conclusion:** The advantages of this method for analytical purposes lie in the rapid determination, its cost-effectiveness, easy preparation of the sample and good reproducibility. In addition to this, the present method can be recommended for the simultaneous determination of Adapalene and Dapsone in routine quality control analysis in combined drug formulations.

INTRODUCTION: Dapsone is also known as 4, 4'- Diaminodiphenyl sulfone **Fig. 1**. Its molecular formula is $C_{12}H_{12}N_2O_2S$ and molecular weight is 248.30 g/mol [1]. Its logP value is 0.97 and pKais 2.41. Dapsone is a white to creamy-white crystalline, odourless powder with a slightly bitter taste. It is active against a wide range of bacteria but mainly used for its actions against Mycobacterium leprae [2] and prescribed in the treatment of leprosy in combination with rifampicin and clofazimine. Additionally, it is used in the treatment of skin related problems.

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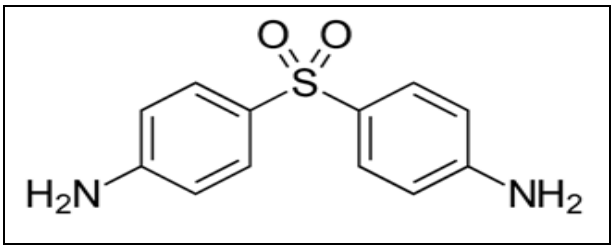

FIG. 1: CHEMICAL STRUCTURE OF DAPSONE

Its mechanism of action is similar to sulfonamides. Dapsone competes with the para-amino benzoate for the active site of dihydropteroate synthase and inhibits dihydrofolic acid synthesis [3]. It is official in IP, BP, and USP [1, 4, 5]. Adapalene is a 6-[3-(1-Adamantyl)-4-methoxyphenyl]-2-naphthoic acid. The molecular structure of Adapalene is as follows (fig 2). Its molecular formula is $C_{28}H_{28}O_3$, and the molecular weight is 412.5 g/mol [6]. It is a third-generation retinoid with a log P of 8.6 and pKa of 3.99.

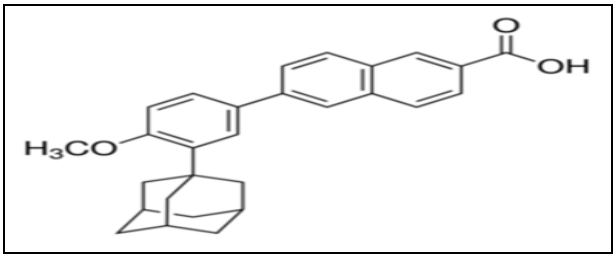

FIG. 2: CHEMICAL STRUCTURE OF ADAPALENE

Adapalene is topically used in the treatment of acne [7]. Adapalene binds to specific retinoic acid nuclear receptors (gamma and beta) and retinoids X receptors but does not bind to the cytosolic receptor protein. The exact mechanism of action of Adapalene is unknown, it is suggested that topical Adapalene may normalize the differentiation of follicular epithelial cells resulting in decreased microcomedone formation.

A combination of Dapsone and Adapalene is used to treat Acne (pimples). A combination is available as a gel formulation in the market. A thorough literature survey revealed that there are UV-Visible spectroscopic methods reported for Dapsone and Adapalene as a single drug [2, 8].

Also, there are some HPLC [3, 6, 9-11,] and HPTLC [12, 13] methods are reported for Dapsone and Adapalene as single drug and in combination with other drugs. But there is no scientific reporting of UV-Visible spectroscopic method for simultaneous estimation of Dapsone and Adapalene in a combined dosage form. Therefore, the objective of current study is to develop and validate the UV-Visible spectroscopic method for the simultaneous analysis of Dapsone and Adapalene in pharmaceutical formulation.

MATERIALS AND METHODS:

Instruments: UV-Visible Spectrophotometer (Shimadzu-1800, Japan) with 10 mm matched quartz cells and Electronic balance (Shimadzu AUX 220) were used.

Reagents and Chemicals: Methanol (AR), Tetrahydrofuran (AR), Distilled water. Details of formulation used for analysis is as follows,

Brand Name: Acnewar plus gel 14

Manufacturer: Akumentis Healthcare Ltd

Composition: Dapsone (5% w/w) + Adapalene (0.1 % w/w)

Experimental Work, Results and Discussion:

Method Development: Selection of solvents: Solubility test for the drug Dapsone and Adapalene was performed by using various solvents.

The solvents include water, methanol, ethanol, acetonitrile, chloroform, and tetrahydrofuran. Dapsone was found to be soluble in methanol, ethanol, 1M HCl, tetrahydrofuran, and Adapalene was found to be soluble only in tetrahydrofuran. Therefore, tetrahydrofuran was selected as a solvent for analysis. Further, required dilutions were done with methanol and distilled water.

Preparation of Standard Stock and Working Standard Solutions: 10 mg of standard drug Dapsone and Adapalene were accurately weighed and dissolved in 5 ml tetrahydrofuran separately into 10 ml volumetric flasks. Finally, volume was made up to the mark with the same solvent to make 1000 µg/ml stock solution.

1 ml of this stock solution of each drug was diluted to 10 ml with methanol to get 100 µg/ml solutions separately. The solutions were further diluted with distilled water to get desired concentrations of 2.5-12.5 µg/ml of Dapsone and 0.05-0.25 µg/ml of Adapalene separately.

Selection of Wavelength and Method of Analysis: A solution of 10 µg/ml of each drug was scanned in the range of 200-400 nm separately using distilled water as a blank.

The wavelengths corresponding to maximum absorbance were noted at 237 nm λ_{max} of Adapalene and 293 nm, λ_{max} of Dapsone, respectively **Fig. 3** and **4**.

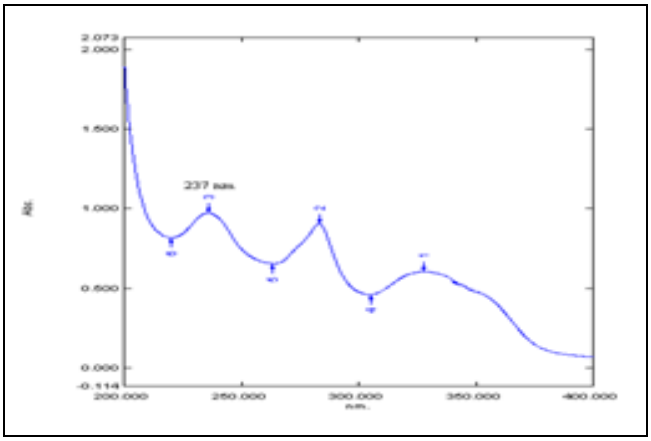

FIG. 3: λ_{max} OF ADAPALENE AT 237 NM

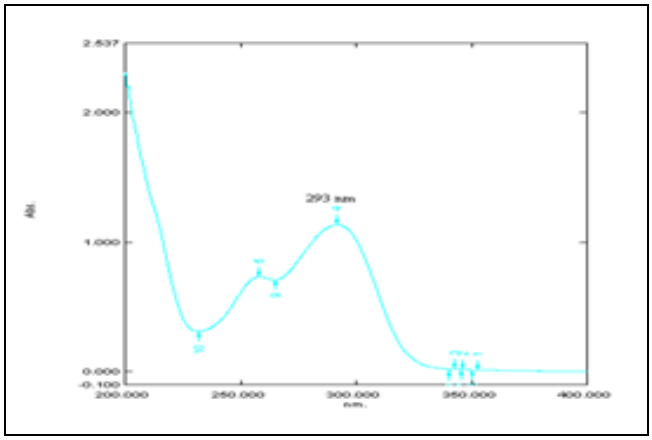

FIG. 4: λ_{max} OF DAPSONE AT 293 NM

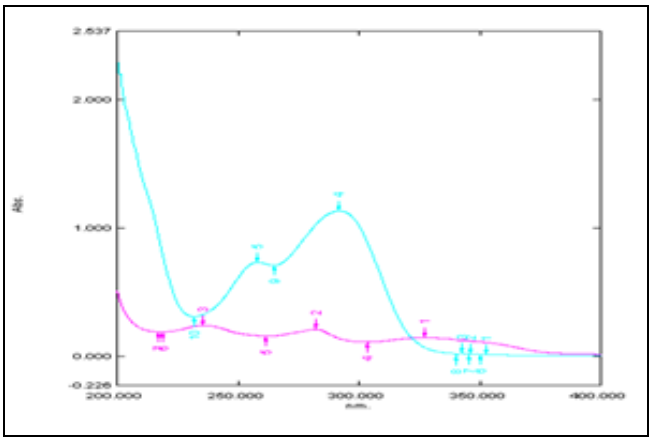

FIG. 5: OVERLAY OF ADAPALENE AND DAPSONE

From the overlay spectrum, the simultaneous equation method was chosen for analysis **Fig. 5** [15].

Simultaneous Equation Method: The gel sample solution was subjected to analysis by the simultaneous equation method.

The absorbances of sample solutions were recorded at 237 nm, and 293 nm and the concentration of two drugs in the sample were determined by using equations 1 and 2.

Equation 1: Simultaneous equation for the estimation of Adapalene

$$Cx = (A2ay1-A1ay2/ax2ay1-ax1ay2)$$

Equation 2: Simultaneous equation for the estimation of Dapsone

$$Cy= (A1ax2-A2ax1/ax2ay1-ax1ay2)$$

Where: ax1= Absorptivity of Adapalene at 237 nm, ax2 = Absorptivity of Adapalene at 293 nm, aY1 = Absorptivity of Dapsone at 237 nm, ay2 = Absorptivity of Dapsone at 293 nm

A1 and A2 are the absorbances of diluted samples at 237 nm and 293 nm, respectively.

Determination of Absorptivity Values: The standard working solutions containing 2.5-12.5 µg/ml of Dapsone and 0.05-0.25 µg/ml Adapalene separately were scanned, and absorbances were measured at selected wavelengths.

From the absorbances and concentrations, absorptivity values (a) were determined. The values were found to be (ax1= 0.144, ax2= 0.0694, ay1= 0.0344, ay2 = 0.1167)

Method Validation: Validation is a process of establishing documented evidence, which provides a high degree of assurance that a specific activity will consistently produce the desired result or product meeting its predetermined specifications and quality characteristics [2, 16].

The validation for UV method development was performed using parameters like linearity, accuracy, precision, specificity, and robustness. The method was validated as per ICH guidelines [16].

Linearity and Range: The linear relationship between absorbance and concentration of the drugs was evaluated in three replicates over the concentration range 0.05-0.25 µg/ml of Adapalene and 2.5-12.5 µg/ml of Dapsone as mixture at selected wavelengths.

The calibration curves were plotted. A well correlated linear fit graph was observed for both the drugs in the concentration range studied **Fig. 6**. The linearity results are shown in **Table 1**.

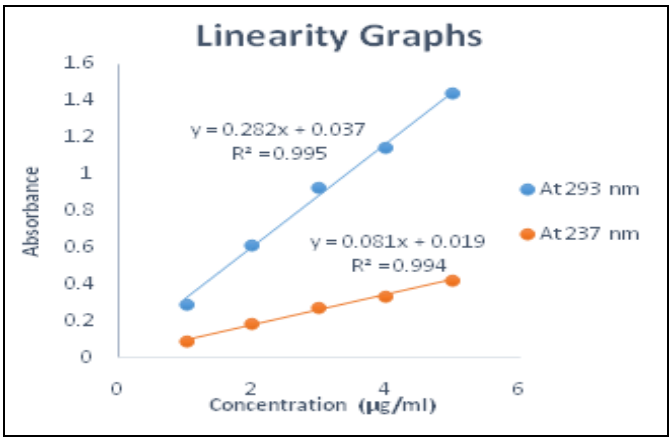

FIG. 6: LINEARITY GRAPH OF DAPSONE AND ADAPALENE

TABLE 1: LINEARITY RESULTS FOR PROPOSED METHOD

Parameters	At 237 nm of Adapalene	At 293 nm of Dapsone
Linearity range (µg/ml)	0.05-0.25	2.5-12.5
Regression equation	y = 0.0818x + 0.0192	y = 0.2827x + 0.0377
Intercept (c)	0.0192	0.0377
Correlation coefficient	0.9946	0.9959

Accuracy: Accuracy of the method was calculated as the percentage recovery. Recovery studies were carried out by preparing synthetic mixtures of the product components containing known quantities of drugs at different levels (75%, 100% and 125%).

Resultant samples were analyzed by the developed method. The amount of drug added and percentage recovery was calculated in **Table 2**.

TABLE 2: RECOVERY RESULTS FOR ADAPALENE AND DAPSONE

Drug	% Recovery Level	Amount added (mg)	Amount recovered (mg)	% recovery	± SD	% RSD
Adapalene	75%	0.15 mg	0.149	99.29	1.481	1.491
	100%	0.20 mg	0.202	100.95	1.957	1.939
	125%	0.25 mg	0.251	100.41	1.397	1.391
Dapsone	75%	7.50 mg	7.61	101.42	0.263	0.259
	100%	10.00 mg	10.19	101.96	0.050	0.049
	125%	12.50 mg	12.72	101.77	0.036	0.035

Precision: Repeatability and intermediate precision of the developed method were expressed in terms of the relative standard deviation of the % drug content.

The sample solution containing 0.2 µg/ml of Adapalene and 10 µg/ml of Dapsone was analyzed in six replicates on the same day for repeatability and on three successive days in triplicates for intermediate precision.

Percentage RSD values were found to be 0.59 and 1.17 for Adapalene; 0.258 and 0.38 for Dapsone for repeatability and intermediate precision, respectively **Table 3** & **4**, confirmed that the precision of the method was acceptable.

TABLE 3: REPEATABILITY RESULTS FOR ADAPALENE AND DAPSONE

S. no.	Adapalene drug content	Dapsone drug content
1	97.51	103.52
2	97.95	103.77
3	97.25	104.12
4	96.75	103.87
5	97.70	104.37
6	98.45	104.02
Average	97.60	103.94
±SD	0.5844	0.2689
% RSD	0.59	0.258

Specificity: The drugs Dapsone and Adapalene in the formulation were accurately quantified using developed method indicated that there was no interference from commonly present excipients and additives.

TABLE 4: INTERMEDIATE PRECISION RESULTS FOR ADAPALENE AND DAPSONE

S. no.	Adapalene drug content	Dapsone drug content
1	99.15	103.67
2	99.64	103.92
3	98.45	104.02
4	100.50	104.40
5	100.50	103.82
6	99.50	104.70
7	97.95	103.77
8	101.50	103.40
9	101.00	103.80
Average	99.79	103.94
±SD	1.1772	0.4001
% RSD	1.17	0.38

Robustness: The prepared standard and sample solution were found to be stable for 8 h.

Assay of Gel: A quantity of gel equivalent to 10 mg of Dapsone was taken in a 10 ml volumetric flask and it was dissolved and diluted up to the mark with tetrahydrofuran. 1 ml of this solution was diluted to 10 ml with methanol. 1 ml of the above was again diluted with distilled water to obtain 10 µg/ml of Dapsone.

The solution was then analyzed by developed UV-Visible spectroscopy method, and the results were indicated by % drug content **Table 5**.

TABLE 5: ASSAY RESULTS OF FORMULATION

Drug	Brand Name	Label Claim	Conc. Prepared	Amount Found µg/ml	% assay	±SD	% RSD
Adapalene	Acnewar Plus	0.1 %	0.2 µg/ml	0.191	95.83	0.6313	0.658
Dapsone	Gel	5 %	10 µg/ml	10.385	103.85	0.3214	0.309

The % drug contents were found to be 95.83 ± 0.6313 and 103.85 ± 0.3214 for Adapalene and Dapsone, respectively.

CONCLUSION: A simultaneous equation UV spectrophotometry method was developed and validated as per ICH guidelines for the determination of Adapalene and Dapsone in a gel formulation. The advantages of the proposed method for analytical purposes lie in the rapid determination, cost-effectiveness, easy preparation of the sample, good reproducibility, simple, accurate, and precise nature. Hence, the proposed method can be recommended for the simultaneous determination of Adapalene and Dapsone in routine quality control analysis in combined drug formulations.

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CONFLICTS OF INTEREST: None

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