RESEARCH ARTICLE

Spectrophotometric Determination of Dapsone in Pharmaceutical Formulation by Schiffs base with p-dimethyl amino benzaldehyde

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Received: 18th September, 2020; Revised: 04th October, 2020; Accepted: 29th November, 2020; Available Online: 25th March, 2021

ABSTRACT

The study includes simple, sensitive, and rapid spectrophotometric method for determination of dapsone (DAP) in aqueous solution. The method is based on the Schiff's base formation which is achieved by coupling of DAP with P-dimethyl amino benzaldehyde (P-DMAB) at pH 2.04 to yield a yellow color product exhibiting maximum absorbance at 454 nm, Beer's law is obeyed in the concentration range 1.6–9.6 µg/mL of DAP, with correlation coefficient 0.9996, with a molar absorptivity 1.8747×10^4 L/mol.cm, sandell´s sensitivity index of 0.0132 µg/cm^2, D.L 0.0390 µg/mL and Q.L 0.1179 µg/mL, RSD, relative standard deviation 0.18–0.36%, the average recovery is 99.49%, the stoichiometric ratio between the drug and reagent 1:2. This method has been applied successfully for determination of DAP in pharmaceutical preparation.

Keywords: Dapsone, p-dimethyl amino Benzaldehyde, Schiff's base, Spectrophotometric Determination.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.1.26

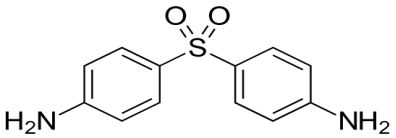
How to cite this article: Ahmad WS, Abdulaziz MS. Spectrophotometric Determination of Dapsone in Pharmaceutical Formulation by Schiffs base with p-dimethyl amino benzaldehyde. International Journal of Drug Delivery Technology. 2021;11(1):141-146.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Dapsone or diaminodiphenyl sulfone (DDS), a sulfones class antibiotic drug[1] reduces swelling (inflammation) and stops the bacteria's development. Generally, it is administered with rifampicin and clofazimine in the treatment of leprosy, elimination half-life 20–30 hours.[2] Dapsone is widely employed as effective antibiotic for prophylaxis agent pneumocystis and an opportunistic disease in (HIV) infection. It has been approved as antibiotic by food and drug administration since 1963. The structural formula is as follows -



Its molecular formula is $C_{12}H_{12}N_2O_2S$, molar mass 248.30 g.mol^{-1} and melting point (175–176°C). Dapsone is widely employed as effective antibiotic for prophylaxis agent pneumocystis and an opportunistic disease in HIV infection. It has been approved as antibiotic by food and drug administration, since 1963.[3] Different methods have been used to for determination of dapsone. It is determined using spectral methods,[4-21] high performance liquid chromatography, chromatographic method[22-26] and Electrochemistry methods.[26-30]

In this study a sensitive and simple spectrophotometric method for determination of Dapsone in pure form and in pharmaceutical formulations based on Schiff's base formation, by the reaction of Dapsone with p-dimethyl amino Benzaldehyde.

EXPERIMENTAL

Apparatus

All spectrophotometric measurements (spectral and absorbance) were carried out on Shimadzu UV-visible 1800 Double beam Spectrophotometer (Japan) using 1-cm matched glass cell was used for recording absorbance. The following instruments were used too: Sartorius BL 2100 balance (German), pH meter 3310 Jenway (German), Water bath (Clifton, USA), Hater with sitter (Heidolph MR3001, German).

Chemicals and Reagents

Analytical grades Chemicals and Reagents were used, and distilled water was used to prepare all solutions throughout. DAP, P-DMAB reagent, were got from FLUKA.

Reagents and Solutions

Dapsones (DAP) solution, 1000 µg/mL, and 200 µg/mL

A stock standard solution containing 1000 µ/mL DAP was prepared by dissolving 0.1000 g of DAP in 1.0 mL of 5 M

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HCl and completed to100 mL volumetric flask filled with distilled water up to mark and kept in dark place, then 200 μ/mL prepared by diluting.

P-dimethyl amino benzaldehyde (P-DMAB) reagent solution (0.01M)

P-DMAB solution 0.01 M was prepared by dissolving 0.1491 g in 0.4 mL of concentrated HCl and then diluted to 100 mL in volumetric flask with distilled water.

Hydrochloric Acid Solution (~1M)

This solution is prepared by diluting 8.47 mL concentrated HCl (11.8 M) to 100 mL volumetric flask with distilled water up to mark.

Pharmaceutical Formulation

Solution of DAP tablets formulation (200 μg/mL) production of Domina Pharmaceuticals (100 mg). The solution (1000 μ/mL) of DAP was prepared by weighing (10 tablets = 1.6472 g) then grounded and taken 0.1 g of DAP and dissolved with distilled water, filtered, washed and filled up to mark in 100 mL volumetric flask, 20 mL from this solution diluted to 100 mL to prepare 200 μ/mL DAP solution.

RESULTS AND DISCUSSION

General Procedure

The principle of the method is based on the Schiff's base formation of DAP with P-DMAB in acidic media to produce yellow colored solution which give maximum absorption at 454 nm.

Preliminary Investigations

A 1.0 mL of p-DMPB 0.01M is added to 1.0 ml standard DAP solution (200 μg/mL) and completed with distilled water in a 25 mL volumetric flask, a yellow color product is obtained with λ max 454 nm against the blank (which the blank not gives any absorption at 454 nm).

Optimization of the Experimental Conditions

The absorption intensity affected by various variables was studied to ensure the optimum conditions, by adding 1.0 mL of P-DMAB 1×10^{-2}M to standard DAP solution (200μg/mL) and measuring the absorption at 454 nm versus the blank.

Effect of the Reagent

Adding 1.0 mL of solutions of 0.01M of different reagents to the volumetric flasks containing 1.0 mL of DAP (200 μg/mL) then the volume is completed to 25 mL with distilled water, and measuring the absorption versus the blank, It is clear that the P-DMAB reagent giving higher absorbance, is the optimum.

Effect of the Amount of Reagent

Adding 1–8 mL P-DMAB (0.01M), to the volumetric flasks containing 1.0 ml of DAP (200μg/mL) and then the addition of 1.0 mL of 1.0 M HCl acid and the volume is completed to 25 mL with distilled water and measuring the absorption at 454 nm versus the blank, it becomes obvious that the volume of 6.0 mL of P-DMAB reagent is the optimum amount because it gave the highest absorbance and hence recommended and adopted in subsequent experiments.

Effect of the Acids and Amount of the Acid

Some of weak and strong acids (1M) have been used 1.0 mL acids with 1.0 mL DAP and 6.0 mL of P-DMAB and found 1 mL of HCl 1M acid give the maximum absorption intensity and this volume was elected in all following measurements.

The results shown in Table 1 indicate that the volume of 1.0 mL of HCl (1M) is the optimum amount because of highest absorbance, so it was used in subsequent experiments.

Effect of Oxidation Time

To a series of volumetric flasks, each containing 6.0 mL of P-DMAB (11×0^{-2} μg/mL) and 1.0 mL of DAP (200 μg/mL) and 1.0 mL (1 M) HCl the solutions are left for different periods of time. The volume is completed to 25 mL with distilled water, and the absorption of solutions is measured at a wavelength of 454 nm versus blank, indicate that the 10 minute is suitable for completion the reaction because of highest absorbance, so it was used in subsequent experiments.

Effect of Temperature

The effect of temperature 5–40°C on the absorption of the formed colored product are studied by using a series of volumetric flasks each containing 6.0 mL of P-DMAB (1×10^{-2} μg/mL) and 1.0 mL of DAP solution (200 μg/mL) and 1.0 mL of HCl (1 M) then the volume is completed to 25 mL with distilled water, and the absorption is measured at a wavelength of 454 nm versus blank. The optimum temperature is 15–30°C, so it is adopted in the subsequent experiments.

Stability of Reaction Product

It was found that the value of absorption of the color product (DAP) 200 μg/mL remained stable for a period of not less than 70 minutes and this time is suitable for completion of many measurements.

Effect of Solvent

After all components of the reaction (6.0 mL of P-DMAB, 1×10^{-2} μg/mL, and 1.0 mL of DAP solution, 200μg/ml, and 1.0 mL of 1M HCl then the volume is completed to 25 mL with distilled water) were added according to the method used, different solvents were used to complete the volume to the extent of up to mark in 25 mL volumetric flask, absorbance measured to obtain that ethanol (E) gives the highest absorption, Table 2 indicates that water is a good medium for

Table 1: Effect of amount of the acid

ml of HCl 1M	without	0.5	0.8	1.0	1.3	1.5	2.0
Abs.	0.506	0.601	0.612	0.620	0.616	0.579	0.539
pH	2.41	2.19	2.11	2.04	1.76	1.64	1.52

Table 2: Effect of solvent

Solvent	*λmax, nm*	*Absorbance*
Ethanol	453.5	0.632
Water	454	0.621
Methanol	455	0.601
Acetone	455.5	0.572

the reaction and gives the highest absorption at wavelength 454 nm, available, economically cheaper.

The results shown in Table 2. Indicate that the ethanol (E) then water (W) gives the highest absorption, so it was used in subsequent experiments.

Procedure Construction of Calibration

Increasing volume (0.2–1.6 mL)~(1.6–12.8 µg/mL) of DAP solution 200µg/mL were added to 25 mL volumetric flask containing 6.0 mL of P-DMAB (0.01 M) and 1 mL of HCl (1M), then complete the volume to the mark with distilled water, left for 10 minutes at 15–30°C and then was measured the absorption of all solution versus Blank solution at 454 nm. Figure 1 represents linear calibration curve for DAP solution with the concentration (1.6–12.8 µg/mL) linear regression equation: y=0.0755x+0.007 (R^2= 0.9996) where y= is the absorbance and x is the concentration in µg/ml. Molar absorption $1.8747x10^4$ $l.mol^{-1}.cm^{-1}$, sandell's Index 0.0132 $\mu g.cm^{-2}$. This indicates that the standard curve has a linear specification and Absorption Spectrum (Figure 1).

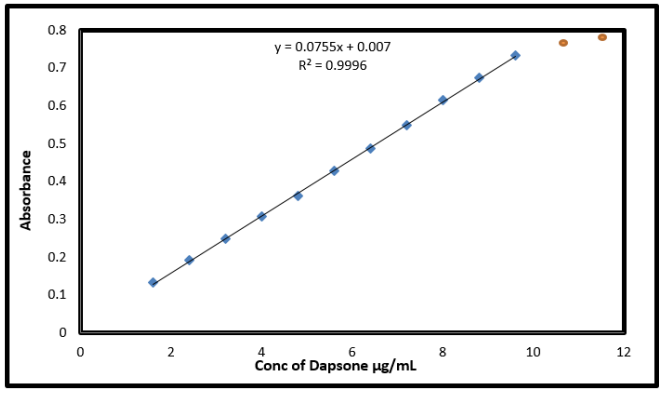


Figure 1: Calibration curve for determination DAP with P-DMAB

Table 3: Analytical parameters

Parameter	*Values*
λ_{max} (nm)	454
Molar absorptivity (l/mol.cm)	$1.8747x10^4$
Beer's Law range ($\mu g.ml^{-1}$)	1.6–9.6
Medium	Acidic
Sandell's Index ($\mu g.cm^{-2}$)	0.0132
LoD ($\mu g.mL^{-1}$)	0. 0390
LoQ ($\mu g.mL^{-1}$)	0.1179
Regression equation	*y = bx+a
Slope (b)	0.0375
Intercept (a)	0.007
Determination coefficient (R^2)	0.9996
Stability (min)	70
Color	Yellow
Average recovery	100.8045%
Average RSD%	0.4661%

y^*= bx+a where y is the absorbance and x is concentration in $\mu g.mL^{-1}$.

Beer's law is obeyed over concentration range of 1.6–9.6 µg/mL.

Analytical Valuation

Under the experimental conditions described, Beer's law, Molar absorptivity (ε) and Sandal's sensitivities for DAP, are given in Table 3. Data of the regression using the least squares method made for calibration curves are also given in the Table 3. The limit of detection (LoD) and the limit of quantum (LoQ) were calculated from calibration graphs using the equation:[31]

$$LOD \text{ or } LOQ = K \times SD/s$$

Were K= 3.3 for LoD and 10 for LoQ, SD is standard deviation of six determinations and **s** is the slope of the calibration curve. LoD is the lower limit of Beer's law range. LoQ is approximately three times greater than LoD.

Accuracy and Precision of the Proposed Method

The accuracy and precision of proposed method were checked by analyzing six replicate samples within Beer's law range containing the same amount of drug. DAP was determined at three different 3.2, 6.4 and 9.6 µg/mL concentrations. The results shown in Table 4. A satisfactory precision and accuracy could be obtained with the proposed method. Average recovery was 99.49. The highest RSD, 0.36%, indicate the good precision and reproducibility of method. The validity of the proposed procedure for determination DAP in its pure state, was tested by analyzing this drug using the proposed method. The proposed method has a good accuracy and precision. The analytical results obtained from this study summarized in Table 4.

Applications of the Method

The proposed method was successfully applied to the determination of DAP in it's pharmaceutical preparation (Domina Pharmaceuticals, 100 mg). The results which are shown in Table 4 indicate that a good recovery was obtained.

Direct Method

In this method, three different concentration of different a pharmaceutical formulation (DAP) solution that are (3.2, 6.4, 9.6 µg/mL) and have done by same way in construction of calibration curve. The absorbance is measured at 454 nm for six times. RE is calculated and the results are shown in (Table 5).

Table 4: Accuracy and precision of the proposed method

Amount of DAP taken, µg/mL	*Amount of DAP measured, µg/mL*	*Relative error*%*	*Recovery* %*	*Average recovery,%*	*RSD* %*
3.2	3.21854	+ 0.58	100.58		0.36
6.4	6.3311	-1.08	98.92	99.49	0.18
9.6	9.5497	-0.52	99.48		0.25

*Average of six determinations and RSD is relative standard deviation.

Table 5: Direct Method for the determination of DAP

Conc. of DAP taken, µg/mL	*Conc. of DAP measured, µg/mL*	*Relative error %*	*Recovery (%)*	*Average recovery (%)*
3.2	3.1656	-1.07	98.93	
6.4	6.3841	-0.25	99.75	99.25
9.6	9.5099	-0.94	99.06	

Table 6: Standard additions Method

Drug of Dapsone (DAP)	*Conc. of DAP taken µg/mL*	*Conc. of DAP measured µg/mL*	*RE*, %*	*Recovery*%*	*Average %*
	3.2	3.2358	1.12+	101.12	100.85
	6.4	6.4365	0.57+	100.57	

*Measurements for six times.

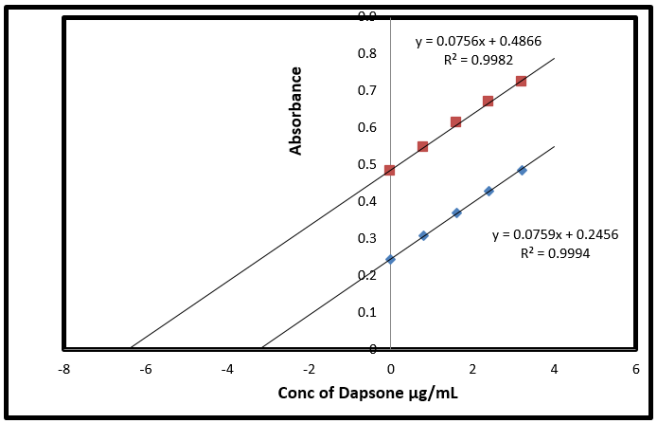


Figure 2: Standard additions method

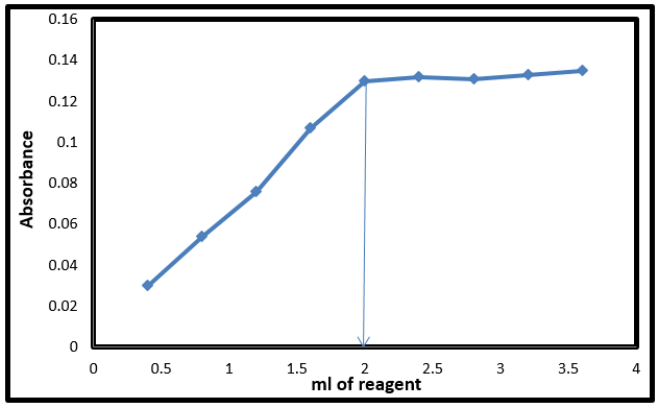


Figure 3: The Mole ratio plots for products of DAP with P-DMAB reagent under the optimum reaction conditions.

The results in Table 13 indicate that good Average recovery 99.25% was obtained.

Standard Additions Method

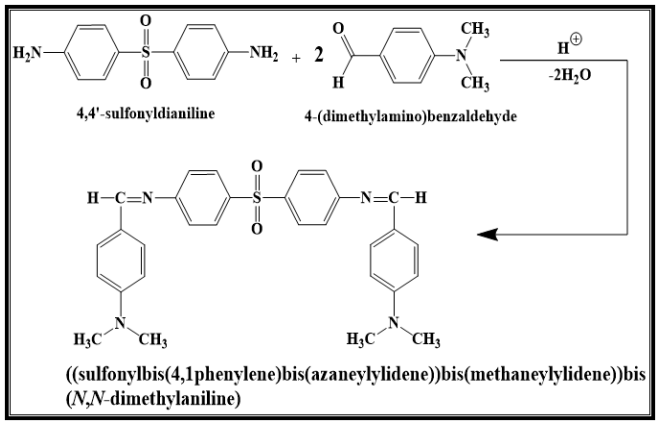
The method of standard additions is applied for determining DAP in its pharmaceuticals to ensure it is free from interference. Different volumes (0.4, 0.8 mL) of a pharmaceutical formulation solution (200 µg/mL) were transferred to six volumetric flasks (25 mL) for each volume, then increasing volumes (0.1–0.5 mL) of 200 µg/mL of DAP standard solution were added with leaving the fifth flask without addition. The solution was treated as in construction of calibration curve. The absorbance was measured at 454 nm (Figure 2) and then measured concentration was calculated from the equation of the straight line and results of Recovery and RE% are shown in the Table 6. Average recovery of five measurements is shown in Figure 2. The results shown in Table 6 indicate that method of standard additions agrees with the direct method within the acceptable.

Stoichiometry of the Complex

The complex's composition had been investigated using Job's method.[31] The method was based on the measurement of series of solutions in which moler concentration of DAP and P-DMAB reagent solution 0.01 M, vary but their sum remained constant, the other solutions added as mentioned in the general Procedure or in the calibration graph. It was found that the drug forms a dye-coupled product with P-DMAB in 1:2 ratio at 454 nm.

The Mole ratio of the complexes formed between the DAP and P-DMAB as a reagent was investigated, the results indicated that 1:2 for DAP with P-DMAB by applying the mole ratio to confirmed Job's method using equimolar solutions of each (1×10^{-2}M). The products were formed in the ratio of 1:2 for DAP and to the reagent P-DMAB (Figure 3)

Therefore the formation of the product probably occurs as shown in Scheme 1 with the spectral methods:



Scheme 1

Some of the physical variables of the proposed method were compared with the differences in the spectral methods from the literature used in the estimation of DAP as shown in Table 7.

The proposed method has been successfully applied in estimating the DAP under study in the pharmaceutical preparations, a good range and sensitivity in compared to other methods.

Table 7: Comparison of methods

Analytical parameters	*Literature method*[9]	*Literature method*[10]	*Present method*
Reagent	Pyrocatechol	Vanilline	P-DMAB
Color	Purple-red	Yellow	Yellow
λ max nm	509	405	454
L/mol.cm)) Ɛ	1.05×10^4	8.69 x 10^3	$\times10^4$1.8747
Beer's law range µg/mL	0.4–20	1–20	1.6–9.6
Sandal Index µg/cm^2	0.0236	0.0286	0.0132
RSD%	1.05–2.60	1.57 >	0.18–0.36
D.L µg/mL	0.0145	0.087	0.0390
Q.L µg/mL	0.05785	0.299	0.1179
Average recovery%	100–101.1	100.39	99.49
Solvent	Water	Water	Water
Ph	2.4	6.13	2.04
Pharm. Preparation	Tablets	Tablets	Tablets

CONCLUSIONS

In this study, a novel spectrophotometric method for determination of trace amounts of DAP has been developed. Which is simple, rapid, accurate and sensitive. Where the method was adopted on Schiff's base formation with P-DMAB in aqueous medium a yellow product dye was obtained at λ_{max} 454 nm. Beer's law is obyed over the range 1.6-9.6 µg.mL^{-1} with a molar absorptivity 1.8747×10^4 l.mol^{-1}.cm^{-1}, Sandell sensitivity index of 0.0132 µg/cm^2. The average recovery is 99.49 % and D.L of 0.0390 µg/mL, Q.L. of 0.1179 µg/mL, relative standard deviation of not more than 0.360 %. It was found that the drug forms a dye-Schiff's base formation product with P-DMAB in 1:2 ratio at 454 nm, and the stablity remain more than 70 minutes. The method was applied successfully for the estimating of DAP in it's pure state or in pharmaceutical preprarations.

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