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A simple method for the spectrophotometric determination of dapsone (diamino diphenyl sulfone-DDS) using new coupling agents in pharmaceutical dosage samples

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Abstract: New coupling agents used for the spectrophotometric determination of dapsone, such as 2-methoxynaphthalene or 6-methyl 2-naphthol is described. These methods are easy, simple and rapid based on the reaction of dapsone with diazotized products of 2-methoxynaphthalene or 6-methyl 2-naphthol to produce a highly coloured azo dyes with maximum absorption at 424 nm and 432 nm. Beers law was obeyed when dapsone coupled with diazotized 2-methoxynaphthalene or 6-methyl 2- naphthol in the range of 0.8 - 22.4 μgmL^{-1} or 1.4 - 25.5 μgmL^{-1}. The molar absorptivity and Sandell's sensitivity, The detection limit (DL) and quantitation limit (QL) of dapsone coupled with diazotized 2-methoxynaphthalene or 6-methyl 2-naphthol azo dyes were found to be 2.979×10^{4} $Lmol^{-1}cm^{-1}$or 2.483×10^{4} $Lmol^{-1}cm^{-1}$, 8.333×10^{-3} μgcm^{-2} or 10.0×10^{-3} μgcm^{-2}, 0.2780 μgmL^{-1}or 0.3027 $\mu gmL^{-1}$and 0.8424 μgmL^{-1}or 0.9174 μgmL^{-1}respectively. The coloured azo dyes formed were stable for five hours. Both the reaction conditions and other analytical restraints were measured. Research has been done on interference from foreign organic compounds. The methods have been successful in identifying dapsone in pharmaceutical drug samples.

Keywords: Spectrophotometry, Diazotization, Dapsone, 2-methoxynaphthalene, 6-methyl 2-naphthol.

1. Introduction

Dapsone is also known as diamino diphenyl sulfone (DDS) or 4, 4'- sulfonyldianiline (SDA) [1]. For the treatment of leprosy, dapsone is frequently combined with rifampicin and clofazimine [2]. DDS was initially investigated as an antibiotic in 1937, and leprosy treatment usage started in 1945[3]. It is included in the WHO's list of essential medications [4]. The oral dosage form is a widely accessible and reasonably priced generic medication [2, 5].

It is a second-line treatment for treating and preventing pneumocystis pneumonia and toxoplasmosis in people with compromised immune systems [2]. It has also been applied to treat dermatitis herpetiformis, acne, and other skin conditions [3]. Blood cell loss, red blood cell destruction, especially in people with glucose-6-phosphate dehydrogenase deficiency, skin rashes, hypersensitivity [2], nausea, appetite loss [6], liver inflammation, and methemoglobinemia [7] are examples of severe side effects.

According to a review of the literature, there are several methods for determining dapsone (DDS) in pharmaceutical samples, including differential pulse anodic voltammetric [8], chromatography [9], HPLC [10], RP-HPLC [11-13], electroanalysis methods [14,15], colourimetric and kinetic method [16], and spectrophotometry [17- 36]. However, some of the methods presented for determining dapsone [8, 14, 16, 22] in pharmaceutical dosage were associated with major flaws such as tedious extraction methods, time consumption, lack of sensitivity, heating issues, and cooling effects.

The diazotization reaction of 2-methoxynaphthalene or 6-methyl 2-naphthol with sodium nitrite in acid medium yields diazonium compounds, which are then coupled with dapsone in alkaline medium yields yellow water-soluble azo dyes. The proposed methods are free of the drawbacks mentioned above and they are risk-free, simple, selective and precise used for the determination of dapsone in pharmaceutical dosage samples by spectrophotometric method.

2. Experimental

2.1 Equipments

A JASCO V-730 spectrophotometer (Serial No. A 023561798) and pH meter (Eutech Instruments pH 510 Serial o. 1398504)

2.2 Chemicals and reagents

Dapsone stock solution (1000 µg mL^{-1}), (Sample from Glaxo SmithKline Pharmaceuticals Limited,

Bangalore, India): Dapsone, 0.102g, was precisely weighed and dissolved in 5 mL of ethanol. The mixture was then transferred to a 100 mL calibrated flask and filled to the proper level with double-distilled water. The working solution was prepared as needed by dilution.

A 0.2 $molL^{-1}$solution of sodium nitrite solution, 0.5 $molL^{-1}$solution of hydrochloric acid solution, 1 % solution of 2-methoxynaphthalene or 6-methyl 2-naphthol solution each, 1 $molL^{-1}$solution of sodium hydroxide solution.

2.3 Dapsone tablets solution (1000 µg mL^{-1})

Dapsone tablets (50mg and 100mg) were obtained from a homegrown dispensary (Glaxo SmithKline Pharmaceuticals Limited, Nashik, Maharashtra) and finely powdered. The dapsone solution was made as previously explained using a precisely measured amount of powder (0.25 g) that was dissolved in 5 mL ethanol, followed by the addition of distilled water, shaken well, and filtered into a 250 mL calibrated flask.

2.4 Procedure for the determination of dapsone

In a series of 10 ml calibrated flasks, an aliquot of the sample solution containing a known quantity of dapsone (DDS). It was then shaken vigorously for 2 minutes with the addition of 1 ml of a 0.2 $molL^{-1}$solution of sodium nitrite and 0.5 mL of a 0.5 $molL^{-1}$solution of HCl before being set aside to allow the diazotization reaction to finish. After that, the mixture was thoroughly mixed after being diluted to 10 ml with double-distilled water and added volumes of 1 mL of 1% 2-methoxynaphthalene or 6- methyl-2-naphthol and 1.0 mL of 1 $molL^{-1}$ NaOH solutions. The formed coloured azo dye's absorbance was measured at 424 or 432 nm after 5 minutes in comparison to the reagent blank.

3. Results and discussion

In the presence of a base, dapsone is coupled with the diazonium salt of 2- methoxynaphthalene or 6-methyl 2-naphthol to produce a coloured azo dye. The absorption spectra of the azo dye produced between dapsone with diazotized 2- methoxynaphthalene or 6-methyl 2-naphthol (Figure 1), having an absorption maximum at 424 nm or 432 nm, respectively. The plot of absorbance versus concentration of dapsone coupled with diazotized 2-methoxynaphthalene or 6-methyl 2-naphthol (Figure 2) and it demonstrates that the dyes obeys Beer's law in the range of 0.8 - 22.4 μgmL^{-1} of dapsone with 2-methoxynaphthalene or 1.4 - 25.5 μgmL^{-1} of dapsone with 6-methyl 2-naphthol and Scheme 1. shows the reaction method.

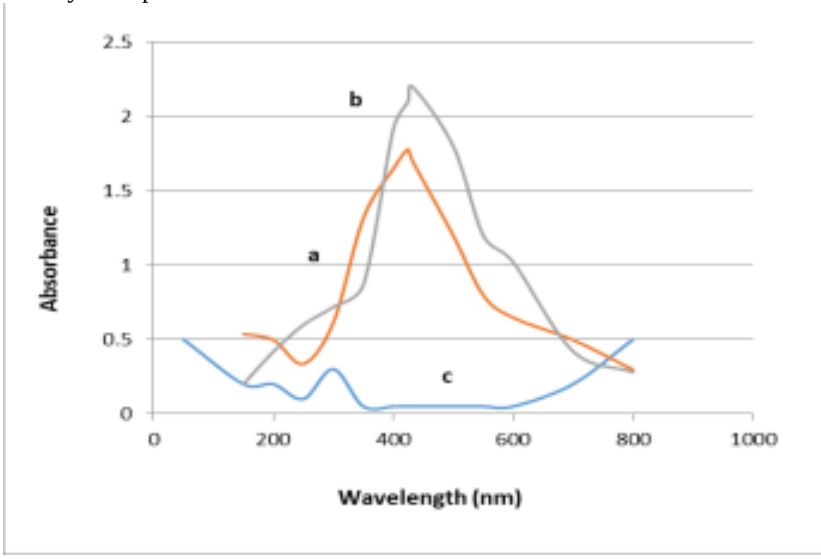


Figure 1 Absorption spectra of the diazocouple of nitrite with 2-methoxynaphthalene against reagent blank (a) Absorption spectra of the diazocouple of nitrite with 6-methyl 2-naphthol against reagent blank (b) reagent blank against distilled water (c).

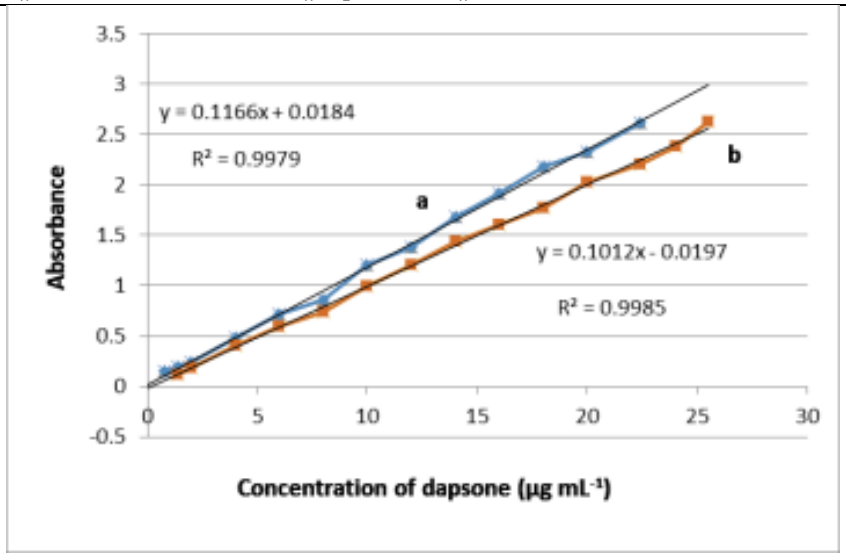
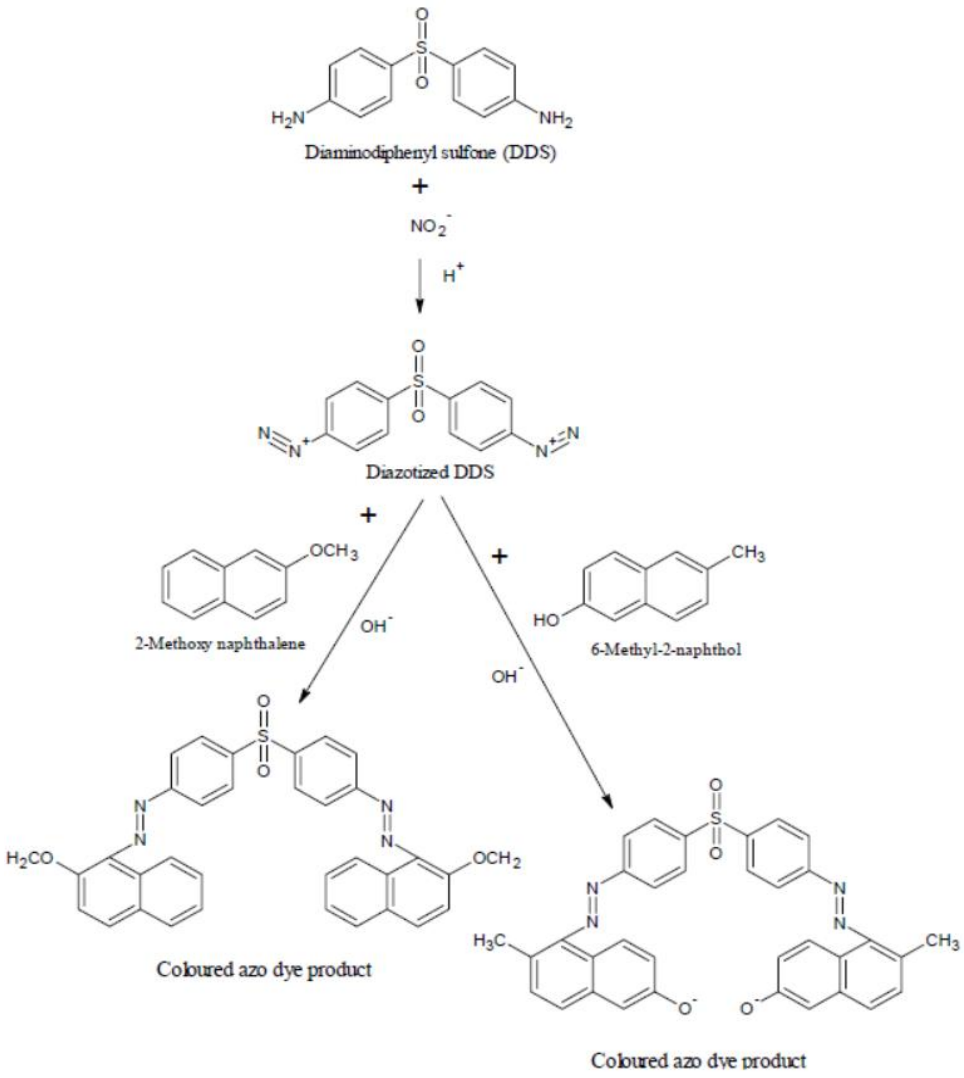


Figure 2 Adherence to Beer's law using dapsone coupled with diazotized 2- methoxynaphthalene or 6-methyl 2-naphthol.



Scheme 1 Diazonium salt of 2-methoxynaphthalene or 6-methyl 2-naphthol is coupled with dapsone to produce coloured azo dyes.

3.1 Effect of Temperature, Acid and Base Concentration

The effect of temperature on diazotization reactions, room temperature (25 ± 5^0C) is advised, because the loss in colour stability and intensity was seen at low and high temperatures.

With the addition of various acid solutions (0.5 mol L^{-1}) and base solutions, the effects of acid and base on the diazotization reaction of dapsone (2µgmL^{-1}) were investigated. (1molL^{-1}). Dapsone produced low absorbance with low colour stability when coupled with diazotized 2-methoxynaphthalene or 6-methyl-2-naphthalene, high absorbance with highest colour stability when combined with HCl, and the highest absorbance when combined with 1.0 mL of NaOH. Therefore, 0.5 mL of 0.5molL^{-1} HCl and 1.0 mL of 1 molL^{-1} NaOH solutions were preferred for the dapsone diazotization reaction.

The maximum absorbance was used to study the effects of various acids (0.5 molL^{-1}), on the diazotization reaction. The volume of each acid was varied between (0.25 and 1.0 mL), while all other variables were held constant. For the diazotization reaction of dapsone, it was discovered that 0.5 mL of 0.5molL^{-1} HCl produced the highest absorbance and was preferred.

3.2 Effect of coupling reagents and nitrite concentration

In the current method, 2-methoxynaphthalene or 6-methyl 2-naphthol is used as a coupling agent by adding 0.50 to 2.0mL of 1% 2-methoxynaphthalene or 6-methyl 2- naphthol to a series of nitrite solutions. In an ultimate volume of 10mL, it was discovered that 1mL of 2-methoxynaphthalene or 6-methyl 2-naphthol (1%) solution produced the brightest and firmest colour.

The colour reaches its peak intensity when using 1mL of 0.2molL^{-1}sodium nitrite solution when using the current method with 2 µgm$L^{-1}$of dapsone and adding 1mL of 0.05-0.40molL^{-1}solutions of the nitrite in hydrochloric acid (0.5molL^{-1}) to a series of nitrite solutions. Lower concentrations produced subpar results, while higher concentrations failed to further increase the absorbance.

3.3 Effect of interference

Several excipients, including urea (200µgmL^{-1}), lactose (500µgmL^{-1}), starch (500µgmL^{-1}), fructose (750µgmL^{-1}) and glucose (1000 µgmL^{-1}), did not interfere with the excipients' determination.

3.4 Analytical data

A straight line is produced on the graph by plotting absorbance versus concentration of dapsone. Beer's law is obeyed between the concentration range 0.8 - 22.4 µgmL^{-1} of dapsone with 2-methoxynaphthalene or 1.4 - 25.5 µgmL^{-1} of dapsone with 6-methyl 2-naphthol. The molar absorptivity of the coloured azo dye of dapsone coupled with the diazonium salt of 2-methoxynaphthalene or 6-methyl 2-naphthol was found to be 2.979×10^4 L$mol^{-1}cm^{-1}$or 2.483×10^4 L$mol^{-1}cm^{-1}$, and the sandell's sensitivity of coloured system with nitrite-2-methoxynaphthalene or nitrite-6-methyl 2- naphthol were found to be 8.333×10^{-3} µgcm^{-2} or 10.0×10^{-3} µgcm^{-2} with maximum absorption at 424 nm and 432 nm.

The regression equation, calibration sensitivity and correlation coefficient (R^2) of dapsone with 2-methoxynaphthalene or dapsone with 6-methyl 2-naphthol were y= 0.1166x + 0.0184 or y= 0.1012x - 0.0197, 0.091 or 0.112, 0.9979 or 0.9985 and have high dye stability (more than 10 h). The detection limit (DL = 3.3/S) and quantitation limit (QL = 10/S) of dapsone coupled with diazotized 2-methoxynaphthalene or 6-methyl 2-naphthol were found to be 0.2780 µgmL^{-1}or 0.3027 µgm$L^{-1}$and 0.8424 µgmL^{-1}or 0.9174 µgmL^{-1}under ideal circumstances, the better optical properties and statistical data were obtained.

3.5 Applications

The provided method is simple and user-friendly and can be used to determine dapsone in a variety of pharmaceutical samples. The results of the suggested methodology closely match the admitted content. The standard deviation ranged from 0.04 to 0.26 for all five samples, and the percentage recoveries ranged from 97.80 to 100.40 with a 95% level of confidence. There were no adverse effects when pharmaceutical samples with additional ingredients appeared. The results are matched to the spectrophotometric method that has been recommended [28]. These confirm that there are no appreciable differences between the proposed method and the suggested method. Replicate analyses were done on five different samples containing dapsone at different concentrations to assess precision and accuracy (Table 1).

Table 1: Determination of dapsone in various pharmaceutical samples

Pharmaceutical Samples	Sample taken ($\mu g\ mL^{-1}$)	Using 2-methoxynaphthalene		Using 6-methyl 2-naphthol	
		Sample found[a] (μgmL^{-1}) ± SD	Rec. (%)	Sample found[a] (μgmL^{-1}) ± SD	Rec. (%)
Dapsone (100 mg/tab)	5.00	4.96 ± 0.08	99.20	4.94 ± 0.06	98.80
	10.00	9.92 ± 0.06	99.20	9.96 ± 0.04	99.60
	15.00	14.84 ± 0.10	98.93	14.88 ± 0.16	99.20
	20.00	19.62 ± 0.14	98.10	19.82 ± 0.18	99.10
Dapsone (50 mg/tab)	5.00	5.02 ± 0.10	100.40	5.00 ± 0.08	100.0
	10.00	9.98 ± 0.04	99.80	9.88 ± 0.16	98.80
	15.00	14.92 ± 0.20	99.47	14.90 ± 0.12	99.34
	20.00	19.56 ± 0.18	97.80	19.74 ± 0.26	98.70

a. Mean (n=5) ± SD {standard deviation}

4. Conclusions

Dapsone was determined spectrophotometrically for the first time using the inexpensive, selective coupling agents 2-methoxynaphthalene or 6-methyl 2- naphthalene. When compared to some of the reported methods, the method is significantly less complicated, faster, more sensitive, reproducible, has good precision and accuracy, and has high dye stability (5 h). Low standard deviation and percentage recovery values highlight the excellent accuracy and precision of the proposed methods and do away with the need for time-consuming solvent extraction or separation processes. The proposed methods produce accurate, repeatable results that are unaffected by excipients. The dapsone analysis in pharmaceutical sample was done using the suggested method.

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