M., **J. Pharm. Clinlq.**, 1997, 16, 189.
7. Szunyog, J., Adams, E., Roets, E. and Hoogmartens, J., **J. Pharm. Bio. Med. Anal.**, 2000, 23, 891.
8. Edberg, S.C. and Miskin, A., **J. Pharm. Sci.**, 1980, 69, 1442.
9. Sampath, S. and Robinson, D.H., **J. Pharm. Sci.**, 1990, 79, 428.
10. Wolfe, S., Ingold, C.F. and Lemieux, R.U., **J. Amer. Chem. Soc.**, 1981, 103, 938.
11. Wolfe, S., Ingold, C.F. and Lemieux, R.U., **J. Amer. Chem. Soc.**, 1981, 103, 940.

Spectrophotometric Determination of 4,4'-Sulphonyldianiline

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A simple, rapid and sensitive spectrophotometric method for the determination of 4,4'-sulphonyldianiline (dapsone) is described. The method is based on the formation of orange red coloured product by the diazotisation of dapsone followed by complexation with dopamine in presence of molybdate ions in 1:1 sulphuric acid medium. The product is stable for two days at 27°. Beer's law is obeyed in the concentration range of 0.1–8.0 μg/ml at 510 nm. The method is successfully employed for the determination of dapsone in tablets and common excipients used as additives in pharmaceuticals do not interfere. The method offers the advantages of simplicity, rapidity and sensitivity without the need for extraction or heating. Limit of detection and limit of quantification are reported.

4,4'-sulphonyldianiline or dapsone (DAP) is used in the treatment of dermatitis herpetiformis[1]. It is used as an antileprotic agent and also as a non-steroidal antibacterial drug. It is also used as an antiparasitic and a commonly used medication for HIV and AIDS patients. An excellent review of pharmacology and therapeutic use of DAP is given by Uetrecht[2]. DAP is also used as a reagent for the determination of various substances[3-6]. DAP is official in British Pharmcopoeia[7,8] and United States Pharmacopoeia[9]. There are various methods available for the determination of DAP, which include HPLC[10-12], liquid chromatography[13], PMR spectroscopy[14], thermometric titration[15] and spectrophotometry[16-22]. The spectrophotometric methods, which have already been reported, suffer from lack of sensitivity, involvement of heating or extraction, longer time taken for completion of reaction and narrow detection limit.

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In the present work, the diazotised DAP is made to react with dopamine hydrochloride (DPH) followed by the addition of sodium molybdate in presence of 1:1 sulphuric acid medium to give an orange red product. This colour reaction is being reported for the first time.

A Jasco Model Uvidec-610 UV/Vis spectrophotometer with 1.0 cm matched cells was used for absorbance measurements. Both DAP and DPH were purchased from Sigma Chemical Co., St. Louis, MO, USA. Molybdic acid was purchased from Merck, Germany and BDH sample of sodium nitrite was used. AR sulphuric acid was used for the experiment. All other reagents and solvents were of analytical grade. Commercial dosage forms were purchased from Burroughs Wellcome.

Deionized water was used to prepare all solutions. Standard solution of DAP (1000 μg/ml) was prepared by dissolving 100 mg of DAP in 2-3 ml of 1.0 M sulphuric acid and

then diluting to the mark in a 100 ml standard flask. A working standard solution of DAP containing 25 μg/ml was prepared by further dilution and standardized by the official method[8]. A 0.2% DPH and 1% sodium nitrite in water were prepared. A 2% molybdic acid (dissolved in 2 ml of 5 M sodium hydroxide and neutralised with dilute hydrochloric acid to get clear solution) solution was freshly prepared. A solution of 1:1 sulphuric acid and 2% aqueous sulphamic acid were used for the experiment.

DAP solution (2.5–120 μg) was transferred into each of the series of 25 ml standard flasks and 2 ml of 1 M sulphuric acid was added to each. After cooling in an ice bath, 2 ml of 1% sodium nitrite solution was added with swirling. The solutions were allowed to stand for 5 min, then 2 ml 2% sulphamic acid solution was added, again swirled and allowed to stand for 5 min. Then 2 ml of 0.2% DPH solution was added followed by the addition of 3 ml of sodium molybdate and left for 5 min to develop pink precipitate. The solution was made up to the mark with 1:1 sulphuric acid and mixed thoroughly. The absorbance was measured at 510 nm against the corresponding reagent blank and a calibration graph was constructed.

Twenty tablets were weighed and finely powdered. The powder amount equivalent to 50 mg was dissolved in 3 ml of 1 M sulphuric acid and filtered. The filtrate was made up to 100 ml and appropriate aliquots of the tablet solutions were treated as described above in the recommended procedure.

The method involves diazotisation of the sulpha drug followed by the addition of dopamine along with molybdate ions to produce pink coloured precipitate, which turns to clear orange red colour after dilution with 1:1 sulphuric acid.

The optical characteristics and precision data are given in Table 1. The colourless reagent blank has practically negligible absorption at 510 nm. It was found that 1 M solution of sulphuric acid in the range of 1-3 ml, 1% solution of sodium nitrite in the range of 1-3 ml, 2% solution of sulphamic acid in the range of 1-5 ml, 0.2% solution of DPH in the range of 1-4 ml and 2% molybdate solution in the range of 2-4 ml were necessary to achieve maximum colour intensity. Hence, 2 ml of sulphuric acid, 2 ml of sodium nitrite and 3 ml of sulphamic acid were used for diazotisation. Two millilitres of DPH and 3 ml of molybdate ions were used to develop the pink coloured precipitate. The excess of nitrite during diazotisation could be removed by the addition of sulphamic acid solution and an excess of sulphamic acid has no effect on colour intensity.

Dilution of the pink precipitate with different solvents like water, methanol, ethanol, acetic acid, hydrochloric acid, sulphuric acid and acetonitrile have been tested. Results showed that 1:1 sulphuric acid dissolves the pink coloured precipitate and turns to orange red colour with maximum intensity and stability. The orange red product was stable for more than two days. The stability of the product resulting from the suggested method was studied in the temperature range of 20-40°. The product was found to be stable for more than 10 h at 40° and the results were reproducible. However, working temperature of 20-30° is excellent for the formation of product and analysis.

Some of the common excipients like starch, talc, gum acacia, sodium chloride, lactose, glucose, dextrose, sodium alginate, carboxymethylcellulose, magnesium stearate (40 mg each) and also vitamin-B_6 (25 mg) do not interfere in the determination of DAP (4 μg/ml). The percentage recovery of DAP in presence of these substances ranged from 99.7 to 100.3 with a maximum relative standard deviation of 0.7% for five determinations. Ions like Cu(II), Ag(I) and

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION DATA.

Parameters / characteristics	DAP-DPH-Mo
Colour	Orange red
λ_{max} (nm)	510
Stability (d)	02
Beer's law range (μg/ml)	0.1-8.0
Limit of detection (μg/ml)	0.1045
Limit of quantification (μg/ml)	0.3482
Molar absorptivity (l/mol.cm)	3.056×10^4
Sandell's sensitivity (μg/cm^2)	0.0081
Optimum photometric range (μg/ml)	0.2-6.0
Regression equation Y = bx+a	
Slope (b)	0.1002
Intercept (a)	0.0204
Correlation coefficient (r)	0.9935
Relative standard deviation (%)	0.45
Range of error	± 0.63

TABLE 2: DETERMINATION OF DAPSONE IN PHARMACEUTICAL PREPARATIONS.

Tablet	Label claim (mg)	Amount of drug found (mg)		
		Proposed method	B.P. method[8]	Reported method[22]
Dapsone	25	24.9±0.7	24.9±0.6	24.8±0.5
	50	50.1±0.6	50.2±0.5	49.8±0.6
	100	99.5±0.7	99.4±0.7	99.3 ± 0.6

Comparative data of the results obtained with analysis of dapsone in tablets by the proposed method with those obtained with the official (BP) and a reported method

CN- interfere. Similarly oxidizing agents like chloramine-T, N-bromosuccinimide and potassium dichromate interfere in the present method. The reproducibility of the method was checked by ten replicate determinations at 4 μg/ml level of DAP and the maximum relative standard deviation (%) was found to be 0.5. The present method has been applied for the analysis of DAP tablets. The results of the analysis of tablets are given in Table 2 and compare favourably with those of the official method[8] and reported method[22]. The percentage relative standard deviation given is for five determinations. The official method[8] for the determination of DAP involves an electrometric titration procedure in the presence of HCl and KBr with $NaNO_2$. The reported method[22] involves diazotisation followed by reaction with cresyl fast violet acetate, which is an indirect determination. The present method is a direct method for the colour development and the lower limit of determination of DAP is 0.1 μg/ml.

The proposed method is found to be simple, rapid and highly sensitive than most of the spectrophotometric methods available in literature. The statistical parameters and the recovery study data clearly indicate the reproducibility and accuracy of the method. The recommended procedure is well-suited for the assay and evaluation of drugs in pharmaceutical preparations to assure high standard of quality control.

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REFERENCES

1. Budavari, S., O'Neil, M.J., Smith, A. and Heckelman, P.E., Eds., In: Merck Index, XII Edn., Merck and Co. Inc., Rahway, NJ, 1996, 478.
2. Uetrecht, J., **Clin. Derm.,** 1989, 7, 111.
3. Sane, R.T., Sawant, S.V., Doshi, V.J., Mhalas, J.G., Paarikh, A.K., Gijare, A.S. and Deshpande, D.S., **J. Assoc. Off. Anal. Chem.,** 1984, 67, 137.
4. Sane, R.T., Ghorpade, U.A., Nadkarni, A.D. and Banavalikar, V.J., **Indian Drugs,** 1986, 23, 306.
5. Sane. R.T., Malkar, V.B., Nayak, V.G. and Sapre, D.S., **J. Assoc. Off. Anal. Chem.,** 1986, 69, 186.
6. Sastry, C.S.P. and Aruna, M., **Indian Drugs,** 1989, 26, 567.
7. British Pharmacopoeia, Vol. 1, HM Stationary Office, London, 1998, 427.
8. British Pharmacopoeia, Vol. 2, HM Stationary Office, London, 1998, 1620.
9. United States Pharmacopoeia XXIV, USP Convention, Inc., Rockville, MD 20852, 2000, 496.
10. Lemnage, M.M., Roenn, A., Flachs, H. and Bygbjerb, I.C., **J. Chromatogr. Biomed. Appl.,** 1993, 613, 340.
11. Moncrieff, J., **J. Chromatogr. Biomed. Appl.,** 1994, 654, 103.
12. Eljaschewitsch, J., Padberg, J., Schuermann, D. and Ruf, B., **Ther. Drug Monit.** 1996, 18, 592.
13. Suhren, G. and Heeschen, W., **Anal. Chim. Acta.,** 1993, 275, 329.
14. Shoukrallah, I.Z.F. and Sakla, A.B., **Spectrosc. Lett.,** 1988, 21, 559.
15. Ajiboye, S.I. and Bark, L.S., **J. Therm. Anal.,** 1989, 35, 1739.
16. Krishna, R.R., Siraj, P. and Sastry, C.S.P., **Indian J. Pharm. Sci.,** 1979, 19, 200.
17. Sane, R.T., Shastri, V.K., Anaokar, P.G. and Nayak, V.G., **Indian Drugs,** 1982, 19, 198.
18. Sanghavi, N.M., Sathe, V.H. and Padki, M.M. **Indian Drugs,** 1983, 20, 341.
19. Zarapker, S.S., Vaidya, S.J. and Lele, R.V., **Indian Drugs,** 1988, 26, 115.
20. Shoukrallah, I., Sakla, A. and Wintersteiger, R., **Pharmazie,** 1990, 45, 675.
21. Shetty, K.T., Naik, P.M. and Mahadevan, P.R., **Indian J. Clin. Biochem.,** 1990, 5101.
22. Sastry, C.S.P., Srinivas, K.R. and Prasad, K.M.M.K., **Anal. Lett.** 1996, 29, 1329.