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Spectrophotometric Determination of Dapsone Using Charge Transfer Complex Formation Reaction

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A SIMPLE, accurate and sensitive spectrophotometric method for the determination of Dapsone has been developed. The method is based on the charge transfer complex formation reaction of dapsone as n-donors with o-chloranil (*o-CA*) as π-acceptor in aqueous medium forming colored complex with maximum absorption at 394 nm. Beer's law was obeyed in concentration ranges of 0.125-1.25 µg/ml with molar absorptivity 1.092×10^5 L. $mol^{-1}.cm^{-1}$. The accuracy of the method (average recovery %) was 100.34% and precision (RSD) ≤ 3.91 %. The results show that complex is formed in ratio 1:2 with the stability constant 3.81×10^9 $l^2.mol^{-2}$. The suggested method was applied successfully to determine Dapsone in its pharmaceutical preparation.

Keywords: Dapsone, Charge transfer complex, o-Chloranil.

Introduction

Dapsone, 4,4'-diaminodiphenylsulfone [I], is a primary treatment for dermatitis herpetiformis. It is an antibacterial drug for susceptible cases of leprosy and pustular psoriasis [1,2] and its effective against various Mycobacterium species [3]. It is a white, odorless crystalline powder, practically in-soluble in water and insoluble in fixed and vegetable oils. Dapsone is issued on prescription in tablets of 25 and 100 mg for oral use [4].

Various analytical techniques have been reported for the determination of Dapsone drug such as chromatography [5,6,7,8], voltammetry [9], and chemiluminescence [10].

Different reagents have been reported for spectrophotometric determination of dapsone, such as, 4-chloro-5,7-dinitrofurazon (11) sodium 1,2-naphthoquinone-4-sulfonic [12] in addition to diazo reactions [13, 14, 15, 16, 17] and UV spectrophotometric method [18,19]. However; molecular interactions between electron donors and acceptors are associated with the formation of colored charge-transfer complexes have absorption bands in the visible region [20, 21]. The aim of the method is to develop an easy, sensitive and cost-effective method.

The present method is development of simple and sensitive spectrophotometric method for the estimation of dapsone, as n-donor, in both pure

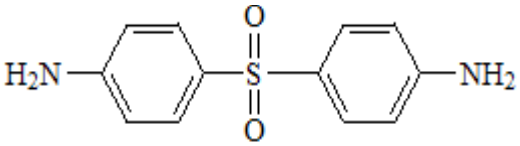

Fig. 1. Dapson structure

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and in pharmaceutical preparations as tablet based on the charge transfer complex formation reaction using o-chloranil reagent as π-acceptor.

Experimental

Apparatus

Shimadzu UV-1800 PC UV-Visible spectrophotometer equipped with a 1.0-cm path length silica cell**,** Philips PW (9421) pH-meter with a combined glass electrode was used for pH measurements**.** All calculations in the computing process were performed in Microsoft Excel for Windows.

Chemicals

All reagents were of analytical-reagent grade which were provided by BDH and Fluka.

Working standard solution Dapsone (100 µg/ml) is prepare by dissolving 0.01g of pure material, provided from Sammara Drug Industries (SDI), in few drops of 0.1M HCl and diluted to the mark in a 100 ml volumetric flask with distilled water. further diluted with water to obtain 25 $\mu g.ml^{-1}$ and kept in refrigerator.

O-Chloranil (*o-CA*) reagent solution (5×10^{3} M) was prepared by dissolving 0.123 g in acetonitrile and diluted to 100 ml in a calibrated flask with the same solvent.

Sodium hydroxide solution (0.01M) was prepared by dissolving 0.1 g in distilled water and diluted to 250 ml in volumetric flask with the same solvent.

Recommended procedure

Aliquots of the working solution of Dapsone were transferred into a series of 10 ml calibrated flasks and diluted to obtain 0.125- 1.25 µg /ml. Then, 1 ml of 5×10^{-3} *o-CA* and 1 ml of 0.01 M NaOH were added and the solutions were diluted to the mark with acetonitrile solvent. The solutions were kept at room temperature (32ºC) for 10 min and the absorbance was measured at 394 nm against reagent blank.

Pharmaceutical Preparations

Ten tablets (each tablet containing 100 mg Dapsone) were accurately weighed and pulverized. A portion of the fine and homogenized powder equivalent to one tablet was weighed and dissolved in few drops of 0.1 M HCl, then the solution transferred to 100-ml volumetric flask and diluted to the mark with distilled water to get 100 µg/ml solution. From this solution 25 µg / ml was prepared and the procedure as described above was followed.

Results and Discussion

Spectral characteristics

Dapsone as n-donor reacts with *o-CA* as π-acceptor in a basic and organic medium at room temperature to give a yellow colored charge transfer complex, the absorption spectrum of which shows a maximum at 394 nm (**Figure 2**).

Optimization of reaction conditions

The optimum conditions for the formation of charge transfer complex were investigated by varying the parameters one at a time and

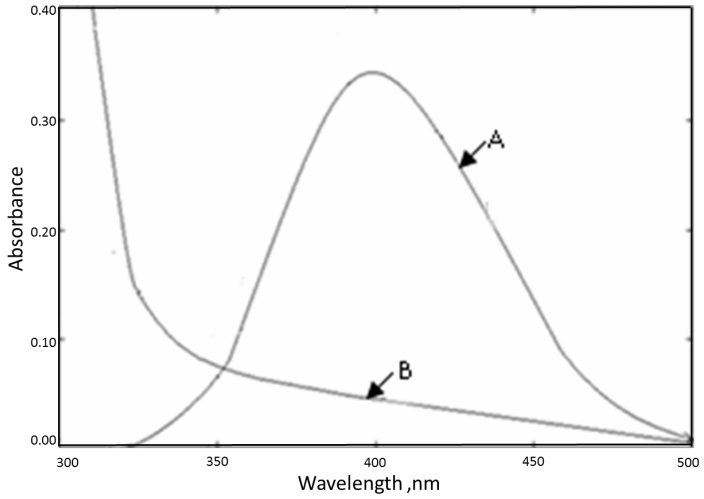

Figure 2 Absorption spectrum of (A) Dapsone (1.0 µg ml-1) with o-CA against reagent blank, and (B) reagent blank against acetonitrile

keeping the others fixed and observing the effect produced on the absorbance of colored species. The following experiments were conducted for this purpose and conditions so obtained were incorporated in general procedure.

Effect of solvents

The formation of a CT complex between donor and acceptor can be affected by the nature of the solvent. Thus, to get the best reaction conditions, solvent nature has been optimized. The absorbance characteristics of the CT complex was examined in various solvents including methanol, ethanol, acetonitrile, acetone and water as medium for the reaction have been tried in order to achieve maximum sensitivity and complex stability.

The absorbance values of the CT complexes in different solvents are shown in Table 1. It was found that on using water as solvent for Dapsone and acetonitrile for *o-CA* in the presence of NaOH and dilution with the acetonitrile was gave maximum color intensity which is recommended in this method. However; dilution with water gave turbid solutions. polar and non-polar solvent can produce a free radicals group which can effect on the stability and sensitivity [22].

Effect of pH and buffer solutions

The effect of pH on the absorption of the complex was studied using different pH values ranged from 2 to12 by using of 0.01 M HCl and NaOH. It was found that the complex was formed at pH of 4.98 by addition of NaOH to the Dapsone (4 µg/ml), **(Figure 3)**. Decrease in absorbance was observed through addition of HCl, which may be attributed to the liberation of hydrogen chloride. Therefore, different buffers of the same pH value are prepared to examine the sensitivity (**Figure 4**). However, a negative effect was observed on the color intensity so only NaOH has been used.

Effect of base

To obtain high sensitivity for the complexes, different bases such as sodium hydroxide, potassium hydroxide, sodium carbonate and sodium bicarbonate with fixed volume and a concentration of 0.01M were examined by addition to a fixed amount of dapsone. It was found that sodium hydroxide gave maximum color intensity (**Figure 5**),and the optimum amount of this base was found to 1.0 ml (**Figure 6**), which was used in the subsequent experiments.

Effect of o-CA concentration

The effect of changing the o-CA concentration on the absorbance of solution containing a fixed amount of dapsone was studied. It was observed that the absorbance increases with increasing *o-CA* concentration and reached maximum on using 1.0 ml of 5×10^{-3}M *o-CA* (**Figure 7**). Therefore, this volume was used in the subsequent work.

TABLE 1. Effect of solvent on the absorbance of charge transfer complex

Blank Absorbance	Sample Absorbance	λ max	Dilution by	O-Chloranil dissolve in	Dapsone dissolve in
Turbid	Turbid	-----	water	water	water
Turbid	Turbid	----	Ethanol	water	Ethanol
0.173	0.299	367	Ethanol	Ethanol	Ethanol
0.423	0.311	318	water	Ethanol	water
0.173	0.257	367	Ethanol	Ethanol	water
Turbid	Turbid	----	water	Ethanol	Ethanol
0.180	0.319	371.5	Methanol	Methanol	Methanol
Turbid	Turbid	----	water	Methanol	water
Turbid	Turbid	----	water	Methanol	Methanol
1.411	0.823	318	Methanol	Methanol	water
0.200	0.342	391.5	Acetone	Acetone	water
Turbid	Turbid	----	water	Acetone	water
Turbid	Turbid	----	water	Acetonitrile	water
0.083	**0.361**	**394**	**Acetonitrile**	**Acetonitrile**	**water**

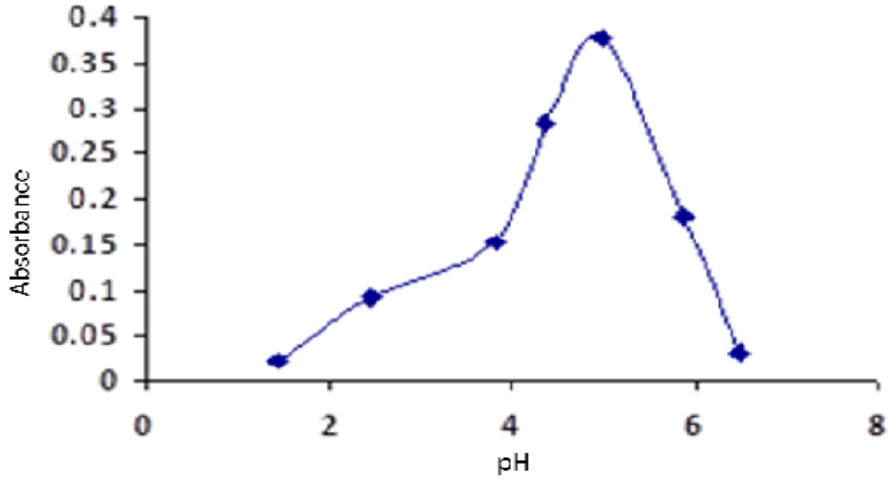

Fig. 3. Effect of pH on the absorbance of charge transfer complex

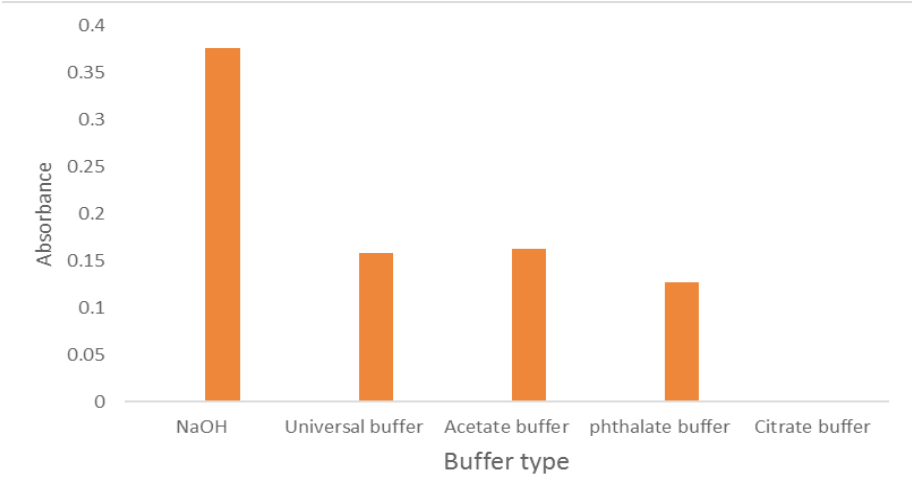

Fig. 4. Buffer type

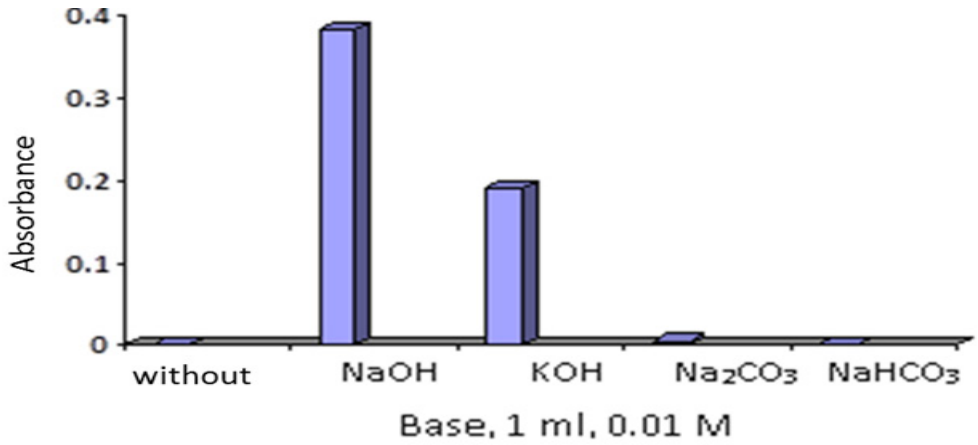

Fig. 5. Effect of base on the absorption of o-chloranil-Dapsone charge transfer complex

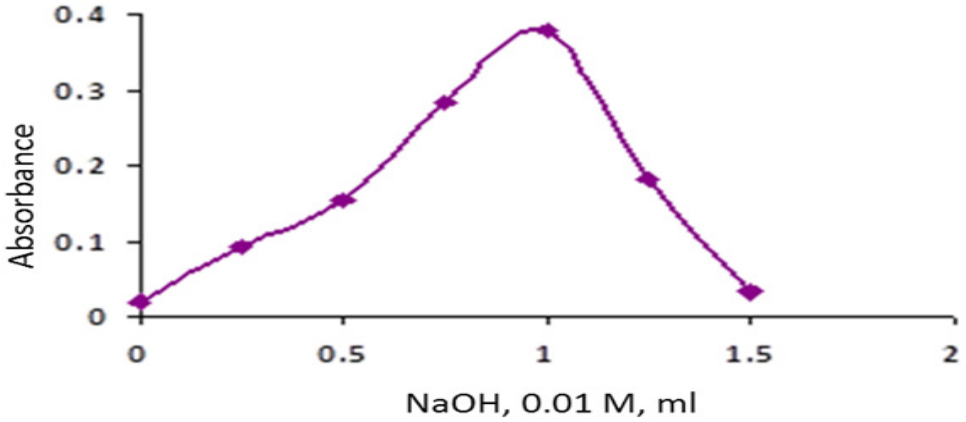

Fig. 6. Effect of NaOH volume on the absorption of 4 µg /ml Dapsone.

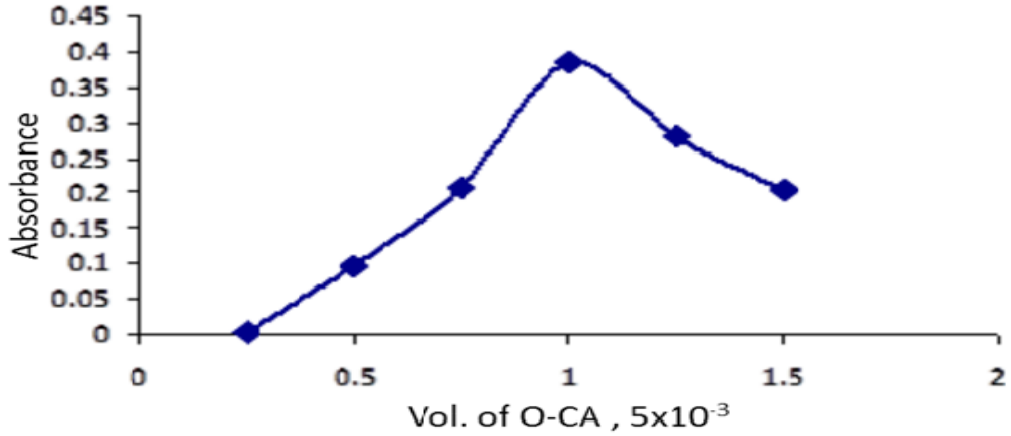

Fig.7. Effect of o-CA concentration on the absorption of 4µg /ml Dapsone.

Effect of temperature and reaction time

The reaction time was determined by following the color development at room temperature and in thermostatically controlled water-bath at different temperatures. The absorbance was measured at 5 and 10 minutes intervals against reagent blank treated similarly. It was observed that maximum absorbance and stability was obtained at room temperature (32°C), 40°C, 50°C and 60°C after 10 min. and remain constant for about 20 min. and the color was fading slowly thereafter. Therefore; room temperature was selected and 10 min was considered for measurement.

Effect of surfactant

Effect of various surfactants including sodium dodecyl sulphate (SDS), cetylperydinum chloride (CPC), cetyltrimethylammonium bromide (CTAB), Tween-80 and Triton x-100 were tested. The results reveal that the presence of the surfactants has negative effect on the intensity of the color. It was found that these surfactants decreased the absorbance of the complexes so surfactant might react with reagent and decrease the concentration of reagent. Therefore, the methods have been carried out without surfactants.

Effect of sequence addition

To obtain optimum results the order of addition of reagents should be followed as given under the general procedure, otherwise a loss in color intensity was observed. As shown in the table below, it is better to add the base after mixing the reagent with drugs. The results are consistent with what was mentioned in literature [23].

Quantification

In order to investigate the range in which the colored complex adhere to Beer's law, the absorbance of the complex was measured at 394 nm after developing the color by following the general procedure for a series of solutions

TABLE 2 Effect of time and temperature on the absorption of complexes

Temperature (°C)	Absorbance/min standing time										
	1.0	5.0	10	15	20	25	30	40	50	60	70
R.T*	0.315	0.376	0.390	0.391	0.390	0.378	0.370	0.357	0.349	0.337	0.332
40	0.314	0.374	0.382	0.391	0.380	0.382	0.371	0.348	0.332	0.328	0317
50	----	0.399	0.393	0.383	0.375	0.370	0.362	0.352	0.332	0.319	0.307
60	----	0.347	0.370	0.340	0.323	0.314	0.308	0.301	----	----	----

*Room Temperature =32 °C

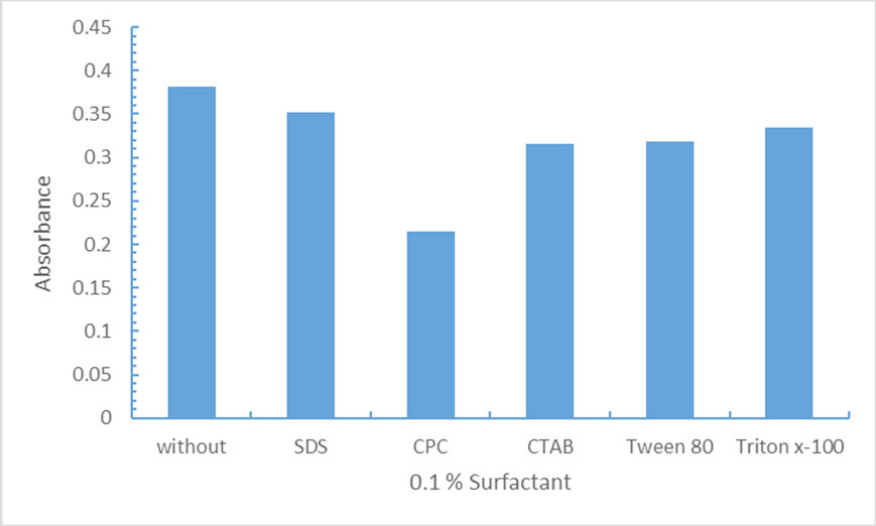

Fig.8. Effect of Surfactant

TABLE 3. order of addition

Sequences addition	Order No.	Absorbance
Dapsone+ Reagent+ Base	1	0.382
Dapsone+ Base + Reagent	2	0.340
Base + Reagent + Dapsone	3	0.033

containing increasing amounts of Dapsone (**Figure 9**). The Beer's law limits and molar absorptivity values were evaluated and given in Table 5, which are indicated that the method could be used for determination of microgram amounts of Dapsone. The linearity was represented by the regression equation and the corresponding correlation coefficient for the studied drug by the proposed method represents excellent linearity. The relative standard deviation (RSD) and accuracy (average recovery %) for the analysis of six replicates of each three different concentrations indicated that the method is precise and accurate. Limit of detection (LOD) are in the accepted range below the lower limit of Beer's law range.

Study of Interferences

The extent of interference by some excipients which often accompany pharmaceutical preparations were studied by measuring the absorbance of solutions containing fixed amount of drug (1 µg/ml) and various amounts of diverse species in a final volume of 5 ml. It was found that the studied excipients did not interfere seriously (Table 5). Slight negative interference was observed in the presence of large excess of excipients. However; an error of 5.0 % in the absorbance readings was considered tolerable.

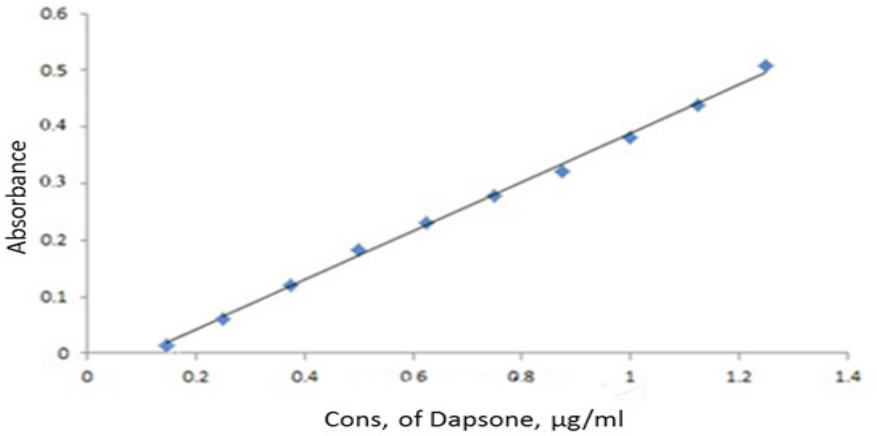

Fig.9. Calibration graph of dapsone

TABLE 4 Summary of optical characteristics and statistical data for the proposed method

Parameter	Value
Beer's law limits (µg/ml)	0.125-1.25
Molar absorptivity	1.092×10^5
LOD (µg/ml)	0.039
LOQ (µg/ml)	0.130
Average recovery (%)[a]	100.34
Correlation coefficient	0.9995
Regression equation (Y)[b]	
Slope, a	0.44
Intercept, b	-0.0408
RSD [b]	≤ 3.91

Analytical application

The proposed method was successfully applied to determine Dapsone in its pharmaceutical preparation as tablet. The obtained results were compared statistically by student's t-test for accuracy and a variance ratio F-test for precision with the official method [24], which was depending on potentiometric titration for dapsone tablet, at 95% confidence level with six degrees of freedom. As cited in Table 6, the result showed that the t- test and F-test were less than the theoretical value (t= 2.57, F= 5.05), indicating that there was no significant difference between the proposed method and official method.

Stoichiometry, stability constant and mechanism

The molar ratio of the complex formed between the Dapsone and *o-CA* reagent was investigated by applying the mole ratio method, using equimolar solutions of each (5×10^{-4} M). The results indicated that the product was formed in the ratio of 1:2 Dapsone: *o-CA* (**Figure 10**). This finding supports that The two NH_2 groups present in dapsone were sharing in the formation of charge-transfer complex.

The apparent stability constant was estimated by comparing the absorbance of a solution containing stoichiometric amounts of the drug and *o-CA* (As) to one containing an excessive amount of *o-CA* reagent (Am). The average conditional stability constant of the complex was calculated, according to the 1:2 ratios, by the following equation:

$$Kc=1-\alpha/ 4\alpha^3 C^2$$

$$\alpha=Am-As/Am$$

Where Kc is the stability constant ($l.mol^{-1}$), α the dissociation degree and C the concentration of the complex which is equal to the concentration of drug. However; the average of stability constant

TABLE 5. Effect of excipient on the determination of 1 µg/ml dapsone

Excipient	Recovery % of 1 µg/ml dapsone per µg/ml exciepient				
	10	25	50	100	250
Sodium chloride	97.00	99.30	98.90	97.32	89.36
Arabic gum	99.82	98.81	100.20	99.00	87.63
Starch	101.06	101.34	100.09	94.86	86.68
Acacia	100.27	99.29	97.31	99.69	85.00
Glucose	100.81	101.62	102.68	100.10	89.15

TABLE 6. Assay of Dapsone in tablet using the proposed method and comparison with the official method

Procedure applied	Pharmaceutical preparation	Drug amount present (µg. ml^{-1})	Recovery (%)	Average recovery (mg)	Certified value (mg)	RSD[a]
Proposed method	**Dapsone[c] Tablet**	0.375	100.53	101.52 (0.17,1.62)[b]	100	1.28
		0.625	102.72			
		1.125	101.51			
Official method	**Dapsone Tablet**	250(mg)	99.36	100.07	100	1.24
			101.84			
			100.85			

a= Average of four determinations, b= Figures in parenthesis are the calculated values for t and F tests respectively, c = Domina pharmaceuticals, Damascus

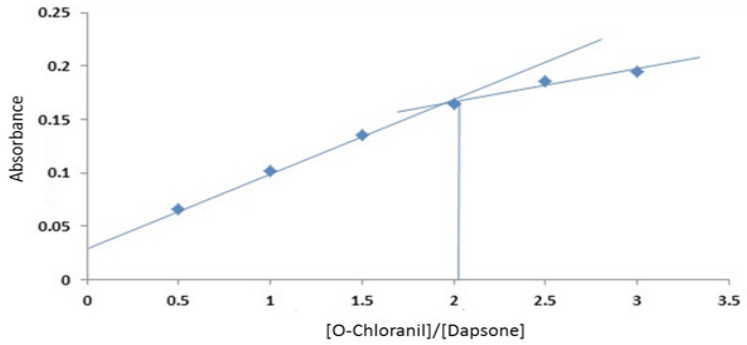

Fig. 10. Mole ratio plot for complex of dapsone with o-CA reagent

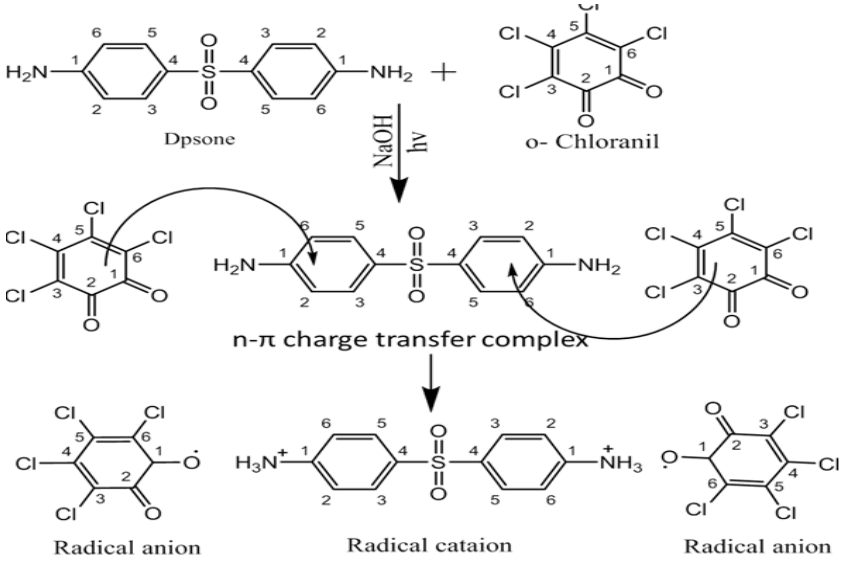

Fig. 11. Proposed mechanism of o-chloranil-Dapsone charge transfer complex formation reaction.

for three different concentrations was found 3.81×109 $l^2.mol^{-2}$ indicating the high stability.

The interaction of dapsone with *o-CA* was a charge-transfer complexation reaction between the n-donor drug and the π-acceptor (*o-CA*), followed by the formation of a radical anion. Complete electron transfers from the donor to the acceptor moiety took place with the formation of intensely colored radical ions with high molar absorptivity values. However; according to the stoichiometric result obtained above, the mechanism reaction may be as **Figure 11**.

References

1. Tiwari R, Tiwari G, Wal P, Wal A, Maurya P., Development, characterization and transdermal delivery of dapsone and an antibiotic entrapped in ethanolic liposomal gel for the treatment of lapromatous leprosy. The Open Nanomedicine J. **5**, 1-15 (2018).

2. Sheu J S, Divito S J, Enamandram M, Merola J F., Dapsone therapy for pustular psorias Case series and review of the literature. Dermatology .**232**, 97–101 (2016).

3. Li, H. Z., Ma, S. H., Zhang, H. M., Liu, J. M., Wu, Y. X., Cao, P. Q., & Gao, X., Nano carrier mediated co-delivery of dapsone and clofazimine for improved therapeutic efficacy against tuberculosis in rats. *Biomedical Research*, *28*(3), 1284-1289 (2017).

4. Kannan, G., Vasantha, J., Rani, N. V., Thennarasu, P., Kousalya, K., Anuradha, P., & Reddy, C. U., Drug usage evaluation of dapsone. *Indian journal of pharmaceutical sciences*, **71**(4), 456 (2009).

5. Salama, N., Ries, M., Toubar, S., Hamide, M. and Walash, M., Validated TLC and HPLC stability-indicating methods for the quantitative determination of dapsone. *JPC-Journal of Planar Chromatography-Modern TLC*, **25**(1), 65-71 (2012).

6. Kaklamanos, G. and Theodoridis, G., Determination of dapsone in muscle tissue and milk using high-performance liquid chromatography–tandem mass spectrometry. *Journal of agricultural and food chemistry*, **60**(1), 29-35 (2011).

7. Colomé, L.M., Freitas, G.M., Bastiani, J.D.M., Pereira, T.C.B., Bajerski, L., Bender, E.A. and Haas, S.E., Validation of analytical method by HPLC for determination of dapsone in polymeric nanocapsules based on crude rice brain oil. *Journal of Applied Pharmaceutical Science*, **7**(07), 230-233 (2017).

8. Gandhi SV, Rathi MS., Development and validation of stability indicating HPLC method for estimation of dapsone. Int. J Pharma Res Health Sci. 6 (2), 2517-2521 (2018).

9. Afkhami A, Gomar F, Madrakian T., Electrochemical sensor for dapsone using molecularly imprinted polypyrrole membrane as a recognition element., J Electrochem Soc. 6)**162**), B109-B113 (2015).

10. Lu, F., Yang, J., Sun, M., Fan, L., Qiu, H., Li, X. and Luo, C., Flow injection chemiluminescence sensor using core-shell molecularly imprinted polymers as recognition element for determination of dapsone. *Analytical and bioanalytical chemistry*, **404**(1), 79-88 (2012).

11. Evgen'ev, M.I., Garmonov, S.Y., Pogorel'tsev, V.I. and Shakirova, E.F., Determination of 4, 4′-diaminodiphenyl sulfone and its derivatives in biological samples by spectrophotometry and chromatography. *Journal of Analytical Chemistry*, **54**(6), 543-548 (1999).

12. Wang, H.Y., Xu, L.X., Xiao, Y. and Han, J., Spectrophotometric determination of dapsone in pharmaceutical products using sodium 1,2-naphthoquinone-4-sulfonic as the chromogenic reagent. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **60**(12), 2933-2939 (2004).

13. Shetty, K.T., Naik, P.M. and Mahadevan, P.R., A specific colorimetric assay for dapsone in biological fluids. *Indian Journal of Clinical Biochemistry*, **5**(2), 101-109 (1990).

14. Al-Obaidi MT, Al-Sabha TN, and Al-Ghabsha TS., Spectrophotometric determination of nitrazepam and dapsone using vanillin reagent in pharmaceutical preparations. J Edu and Sci, **27** (1), 43-57 (2014).

15. Higgins, T.N. and Taylor, J.D., Colorimetric method for the quantitative determination of Avlosulfon (Dapsone) in serum. *Clinical biochemistry*, **6**, 295-299 (1973).

16. Chakravarthy, I.E. and Reddy, N.R., Spectrophotometric Determination of Dapsone from Pharmaceutical Preparations. *Asian Journal of Chemistry*, **16**(3), 1918 (2004).

17. Revanasiddappa, H.D. and Manju, B., A spectrophotometric method for the determination of metoclopramide HCl and dapsone. *Journal of pharmaceutical and biomedical analysis*, **25**(3-4), 631-637 (2001)..

18. De, A., Dey, S., Pradhan, P.K., Chaudhari, F. and Patel, M.**,** Estimation of dapsone in bulk & dosage form by UV spectroscopic method. *American Journal of Pharm Research*, **4**(01) (2014).

19. Sawsan, A.R.A., Nahla, S.N., Manal, F.M., Shimaa, A.A. and Naglaa, E.K., Spectrophotometric determination and thermodynamic studies of the charge transfer complexation of emedastine difumarate with some π-acceptors. *Arabian Journal of Chemistry*, **10**, S1855-S1861 (2017).

20. Alizadeh, N. and Barari Shahidani, M., Application of Charge Transfer Complexation Reaction for the Spectroscopy Determination of Anticonvulsant Drug Primidone. *Analytical and Bioanalytical Chemistry Research*, **5**(1), 81-93 (2018).

21. British Pharmacopia on CD-ROM., General Medical Council, London (2016).

22. Peover, M.E. and Davies, J.D., Reduction potentials and intermolecular charge-transfer spectra of organic acceptor molecules. Part 3—Solvent effects on p-benzoquinones. *Transactions of the Faraday Society*, **60**, 476-478 (1964).

23. Theia'a, N., Mohammed S. Al-Enizzi, and Omar A. Al-Taee., Application of Chloranil and Fluoranil π-Acceptors for the Spectrophotometric Determination of Mesalamine in Pharmaceutical Bulk and Dosage Forms. European Chemical Bulletin, 4,377-383 (2014).

24. Hargis LG. Analytical Chemistry, principles and techniques. Prentice- Hall Inc. New Jersey, 424 (1988).

تم تطوير طريقة طيفية بسيطة ودقيقة وحساسة لتقدير الدابسون. اعتمدت الطريقة على تكوين معقد الشحنة المنتقلة من تفاعل الدابسون كمادة مانحة للإلكترونات مع أورثو-كلورانيل كمادة مستقبلة للإلكترونات نوع باي في وسط مائي لتكوين معقد ملون يمتلك أقصى امتصاص عند 394 نانوميتر. اتبعت الطريقة قانون بير في مدى التركيز 0.125-1.23 ميكروغرام/ملليتر وبامتصاصية مولارية 1.092×10^{5} لتر.مول$^{-1}$.سم$^{-1}$. بلغت دقة (نسبة الاسترجاعية) 100.34% والتوافقية (الانحراف القياسي النسبي) ≥ 3.91. كما وجد أن المعقد