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Study on the charge-transfer reaction between 7,7,8,8-tetracyanoquinodimethane and drugs

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Abstract

The charge-transfer (CT) reaction between 7,7,8,8-tetracyanoquinodimethane (TCNQ) as a π-electron acceptor and cinnarizine, analgin, norfloxacin as electron donors have been studied by spectrophotometric method. The charge transfer complexes between TCNQ and these drugs have stable blue color, therefore a simple, rapid, accurate and sensitive method for determination of these drugs has been developed. The optimization of the experimental conditions is described. Beer's law is obeyed in the ranges 2–18, 2–18 and 4–32 μg/ml for cinnarizine, analgin and norfloxacin, respectively. The apparent molar absorptivity of CT complexes at 743 nm is 1.58×10^4, 1.71×10^4 and 8.91×10^3 l/mol per cm, respectively. The composition of all these CT complexes are found to be 1:1 by different methods. The relative SDs are less than 3% ($n = 10$). The proposed method has been applied to the determination of these drugs in their each pharmaceutical dosage forms with satisfactory results.

Keywords: Charge transfer reaction; Spectrophotometry; Cinnarizine; Analgin; Norfloxacin; 7,7,8,8-tetracyanoquinodimethane (TCNQ)

1. Introduction

The charge transfer (CT) reaction has been widely studied recently. Many drugs are easy to be determined by spectrophotometry based on color CT complexes formed between some electron acceptors and drugs as electron donors. 7,7,8,8-Tetracyanoquinodimethane (TCNQ) is a strong electron acceptor and has been used for the determination of electron donors such as benzothiadiazine diuretics [1], norfloxacin [2], penicillins [3], terfenadine [4], retinol via [5], isoniazid [6], etc. In the present study, TCNQ is used for determination of cinnarizine, analgin and norfloxacin. These drugs are widely prescribed therapeutic agents. Due to their medicinal importance, several methods have been reported for their determination such as non-aqueous titration [7], UV-spectrophotometry [8–10], high-performance liquid chromatographic [11], polarography [12], iodimetric analysis [13]. The method based on the charge transfer reaction between TCNQ and these drugs is easy and less time consuming comparing with the above methods. In this paper, norflox-

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acin was determined with TCNQ in acetone, which is better than acetonitrile used in literature [2], as acetone is not toxic, and the sensitivity in acetone is higher than that in acetonitrile. The determination results are in agreement with those of official method or literature method.

2. Experimental

2.1. Apparatus

A Shimadzu Model UV-265 double-beam spectrophotometer (Kyoto, Japan) was used for recording absorption spectra, and a Model 724 spectrophotometer (Shanghai, China) for the measurement of absorbance at a given wavelength, using 1-cm cells.

2.2. Reagents

All chemicals and solvents used were of analytical or guarantee reagent grade.

7,7,8,8-Tetracyanoquinodimethane (TCNQ) solution in acetone, 1.00×10^{-2} mol/l (2.04 g/l), (A.R, Aldrich Chemical Company, Inc. USA); standard cinnarizine solution in methanol, 1.36×10^{-4} mol/l (0.050 g/l); standard analgin solution in methanol, 1.56×10^{-4} mol/l (0.050 g/l); standard norfloxacin solution in acetone, 3.14×10^{-4} mol/l (0.100 g/l). All of drug standard samples were obtained from Chinese National Institute for the Control of Pharmaceutical and Biological Products. The commercial formulations of drugs were bought from a local drug store.

2.3. Procedure

2.3.1. General procedure

A suitable amount of drug solution was pipetted into a 5-ml volumetric flask. 2.00 ml of TCNQ solution was added, the solution was diluted to volume with acetone or methanol and mixed thoroughly. The flasks with solution were placed for 10 min for cinnarizine and 5 min for norfloxacin at room temperature, and 30 min in 35°C water bath for analgin, respectively. The absorbance of solution was measured at 743 nm against the reagent blank prepared in the same manner simultaneously.

2.3.2. Procedure for tablets of cinnarizine and analgin

Ten tablets of drugs were weighed and pulverized carefully, certain amount of powder (containing about 50 mg of cinnarizine or analgin) was dissolved well and diluted to mark of 100 ml calibrated flask with methanol. The solution was filtered, the first 10 ml of the filtrate was discarded, the 10 ml of continuation of sample solution was diluted to ten times volume with methanol and was tested as under Section 2.3.1.

2.3.3. Procedure for capsules of norfloxacin

Ten capsules of norfloxacin were weighed and pulverized, certain amount of powder (containing about 100 mg of norfloxacin) was dissolved well and diluted to mark of 100 ml calibrated flask with acetone. The sample solution was filtered and tested as described above.

3. Results and discussion

3.1. Absorption spectra

TCNQ was found to react with these drugs to produce an intensely blue color products — charge transfer complexes. They have absorption peaks at 743 and 845 nm. The absorption spectra in range of 700–900 nm are shown in Fig. 1. These drugs and the TCNQ–acetone have no absorption at the same wavelength range, but the TCNQ–methanol have a slight absorption against methanol solvent, as the methanol also has n-electron and react with TCNQ, so the ratio of solvent component must be constant.

Considering the application range of Model 724 spectrophotometer, we chose 743 nm as measure wavelength.

3.2. Effect of reaction time and temperature

Effect of reaction time was tested at various temperatures (20,25,30,35,40 and 45°C) respectively. The suitable temperature and time for ob-

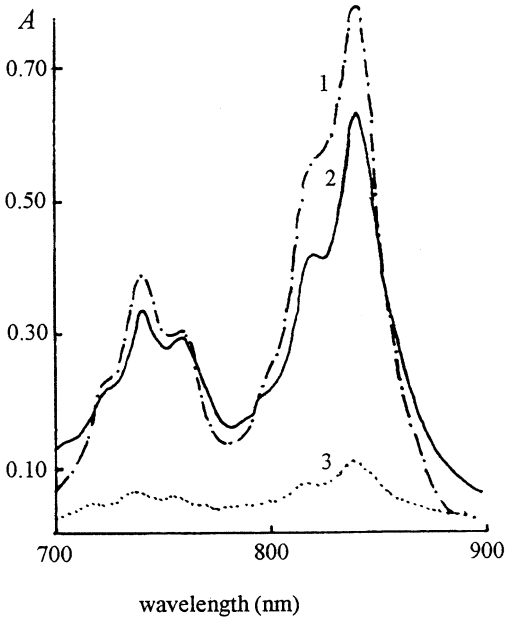


Fig. 1. Absorption spectra: (1) TCNQ–norfloxacin against reagent blank, c(norfloxacin) = 8.4×10^{-5} mol/l, (2) TCNQ–cinnarizine(analgin) against reagent blank, c(cinnarizine) = 3.7×10^{-5} mol/lc(analgin) = 3.5×10^{-5} mol/l, (3) TCNQ–methanol against methanol, c(TCNQ) = 4.00×10^{-3} mol/l.

taining maximum and stable absorbance are shown in Table 1. The stable time of CT complex at room temperature is also shown in Table 1.

3.3. Effect of TCNQ concentration

The amount of TCNQ solution is tested for 1.00 ml standard solution of drugs, respectively. Experiment indicated that 2.00 ml TCNQ solution is enough for each drug (see Fig. 2), the final concentration of TCNQ is 4.00×10^{-3} mol/l.

Table 1
Reaction temperature and time for TCNQ with drugs

Drugs	Cinnarizine	Analgin	Norfloxacin
Reaction temperature (°C)	20	35	20
Reaction time (min)	10	30	5
Stable time (min)	40	60	70

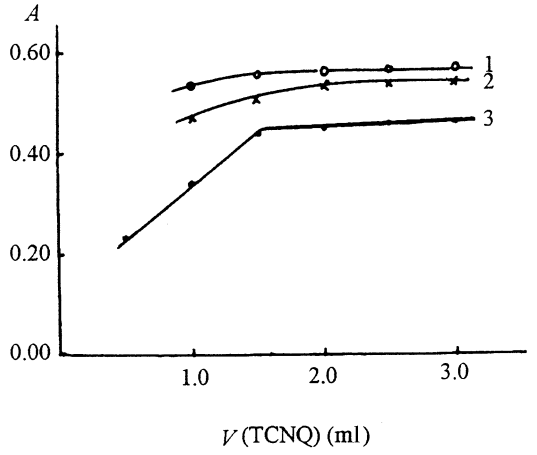


Fig. 2. Effect of the amount of TCNQ: (1) For norfloxacin (6.28×10^{-5} mol/l), (2) For analgin (3.12×10^{-5} mol/l), (3) For cinnarizine (2.72×10^{-5} mol/l).

3.4. Effect of solvent

The solvents studied were: water, ethanol, isopropanol, acetonitrile, acetone, chloroform. Experiment indicated that acetone is the best one for norfloxacin, as it gave the most intense and stable absorbance. A mixed solvent of acetone–methanol is suitable for cinnarizine and analgin. For cinnarizine acetone is profitable, the ratio of acetone to methanol 4:1 as cinnarizine is soluble in methanol. For analgin, methanol is profitable, but TCNQ is easy to dissolve in acetone, the amount of TCNQ acetone solution is a constant 2.00 ml, the ratio of acetone to methanol 2:3.

3.5. Linear range, Precision and Sensibility of method

Under the proposed experimental conditions, the calibration curves were made. The linear regression equation, linear concentration range of drugs, apparent molar absorptivities (ε), Sandell's sensitivities (S) and correlation coefficient (r) are listed in Table 2. The ε of TCNQ–norfloxacin complex is same with that obtained by Alaa S. Amin et al. [2], the linear range is almost same with their (that reported from literature [2] may be some wrong). If the absorbance is measured at 845 nm, the proposed method for drugs should be more sensitive (the ε_{845} is about twice that of ε_{743}).

Table 2
Parameters for determination of drugs ($\lambda = 743$ nm, $n = 9$)

Drugs	Linear regression equation (c) (μg/ml)	Linear range (μg/ml)	ε (l/mol per·cm)	S (μg/cm)	r
Cinnarizine	$A = 0.0143 + 0.0428c$	2–18	1.58×10^4	0.0233	0.9996
Analgin	$A = 0.0006 + 0.0534c$	2–18	1.71×10^4	0.0188	0.9998
Norfloxacin	$A = 0.0024 + 0.0280c$	4–32	8.91×10^3	0.0357	0.9998

To check the repeatability of the method, we prepared ten solutions using 1.00-ml drug standard solution and measured their absorbance respectively. The results are listed in Table 3.

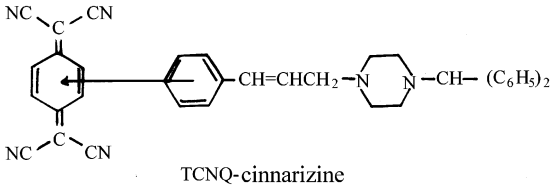
3.6. The composition and stability constant (K) of CT complexes

The composition of all the CT complexes were found to be 1:1 by Bent–French, molar ratio, Job's or curve-cross methods. The results are shown in Figs. 3–6.

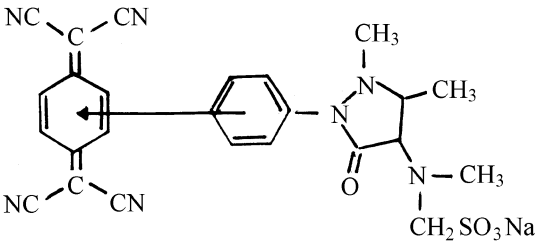
The stability constant (Ig K) of CT complexes are 3.8 for cinnarizine from Fig. 4; 3.9 for analgin from Figs. 4 and 5.; 5.8 for norfloxacin from Figs. 3 and 6.

3.7. Mechanism of reaction between TCNQ and drugs

TCNQ is a electron acceptor, and the benzene ring in molecule of cinnarizine and analgin is the most electron rich group, so a π–π*CT complexes are formed:



TCNQ-cinnarizine



TCNQ- analgin

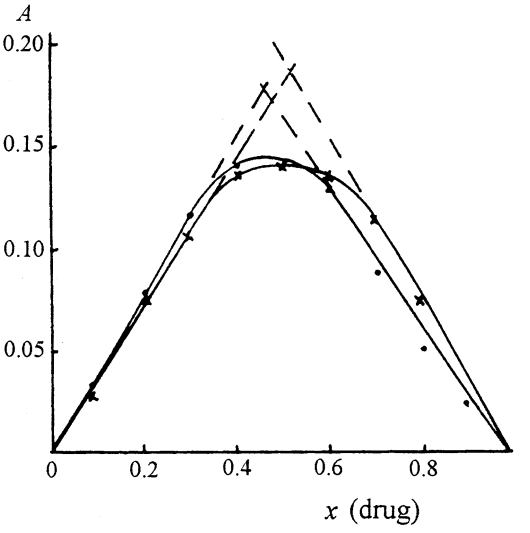


Fig. 3. Determination of composition of complexes by Job's method (×) TCNQ–cinnarizine, $c(\text{TCNQ}) = c(\text{cinnarizine}) = 2.72 \times 10^{-4}$ mol/l, (●) TCNQ–norfloxacin, $c(\text{TCNE}) = c(\text{norfloxacin}) = 3.14 \times 10^{-4}$ mol/l.

Table 3
Check of the repeatability

Drugs	1	2	3	4	5	6	7	8	9	10	RSD%
Cinnarizine	0.462	0.458	0.456	0.455	0.459	0.464	0.461	0.482	0.489	0.449	2.7
Analgin	0.532	0.532	0.539	0.541	0.526	0.535	0.527	0.533	0.535	0.541	0.93
Norfloxacin	0.556	0.562	0.564	0.550	0.547	0.548	0.560	0.565	0.562	0.558	1.2

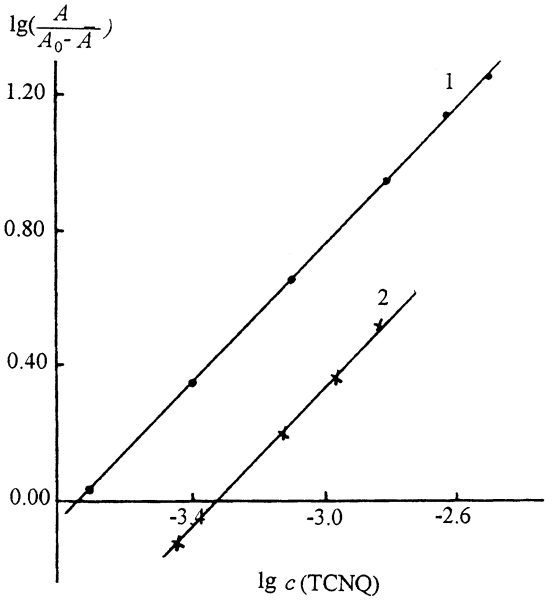


Fig. 4. Determination of composition of complexes by Bent–French method: (1) TCNQ–analgin $y = 1.02\ x + 3.82$ ($r = 0.999$) $K = 10^{3.82}$, (2) TCNQ–cinnarizine $y = 1.14\ x + 3.78$ ($r = 0.995$) $K = 10^{3.78}$.

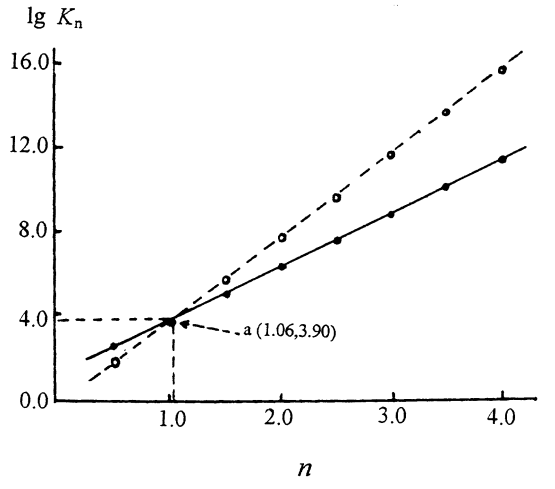
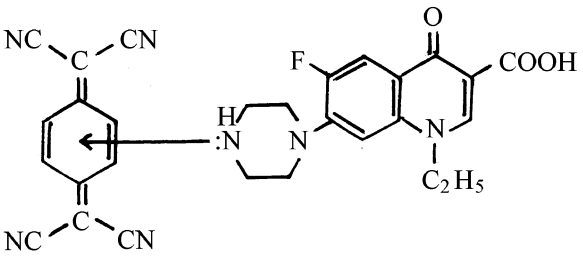


Fig. 5. Curve cross method for composition of TCNQ–analgin complex a (1.06, 3.90) $K = 10^{3.90}$.

In the molecule of norfloxacin, because the presence of the F atom acting as an electron-drawing group, the benzene ring has lower electron density, but the N atom in piperazinyl has more electron density, so the complex formed owing to n–π* transition:



TCNQ-norfloxacin

This mechanism is just like that between norfloxacin and TCNQ [15], however the N atom with lone pair electron is predominant by spatial structure.

4. Analytical application

The proposed method was applied to assay some pharmaceutical formulations. The results are shown in Table 4. Comparison of the results obtained by the proposed method with those obtained by official method or literature method. The accuracy of the proposed method is satisfactory, they are suitable for the determination of main component in drug formulations without interference from excipients such as starch and glucose or from common degradation products.

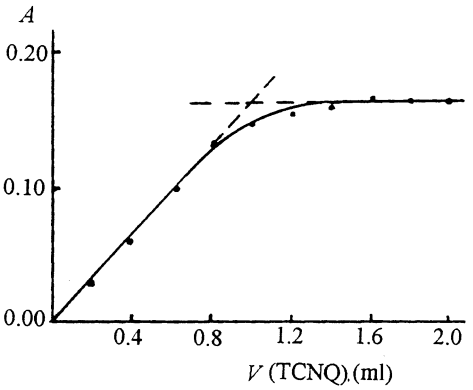


Fig. 6. Molar ratio method for composition of TCNQ–norfloxacin$c(\text{TCNQ}) = c(\text{norfloxacin}) = 3.14 \times 10^{-4}$ mol/l.

Table 4
Determination of drugs in pharmaceutical formulation using TCNQ ($n = 3$)

Drugs	Present method			Official method	
	Found (mg/grain)	Equivalent nominal content (%)	Recovery (%)	Found (mg/grain)	Equivalent nominal content (%)
Cinnarizine	23.55	94.2	99.8	23.50	94.0 [8] (UV method)
Analgin	511	102.2	100	512	102 [13] (iodimetry)
Norfloxacin	99.1	99.1	99.2	98.7	98.7 [14] (chloranil CT)

Acknowledgements

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