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Spectrophotometric and thermodynamic studies on the 1:1 charge transfer interaction of several clinically important drugs with tetracyanoethylene in solution-state: Part one

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ABSTRACT

The occurrence and environmental fate of pharmaceuticals represents a rising and significant public concern worldwide. To provide basic data that can be used to detect and determine several drugs in such environments, this work examines the charge transfer (CT) interaction of tetracyanoethylene (TCNE) as a π-acceptor with eight drugs by spectrophtometry in acetonitrile (MeCN). All of the drugs formed stable yellow compounds with TCNE. The results show that the complexation stoichiometry of TCNE/drug is 1:1. Several spectroscopic and thermodynamic parameters were estimated using the Benesi–Hildebrand and Van't Hoff's equations. Very strong linear correlations were observed between the thermodynamic parameter. The IR data suggest that the complexation between TCNE and drugs occurs *via* n → π* and/or π → π* interactions.

1. Introduction

1.1. Aim of the study

In the last few decades, the presence and fate of pharmaceutical products in the aquatic environments such as natural water represents a rising and a significant public concern worldwide and considered by the scientific community as a new source of pollution. These issues have motivated researchers to investigate and develop fast, simple and efficient methods for the detection and determination of drugs in such samples. One promising technique to achieve this goal is charge transfer (CT) complexation. The chemistry of the CT interaction between drugs and acceptors is attracting considerable interest from chemists and pharmacists, growing in importance in recent years and has become a popular area of research. A number of reasons support the growing attractiveness of this topic, such as (i) Relevant, important topic in pharmacology, chemistry, biology and medicine. (ii) Significant physical and chemical properties of the formed complexes [1–13]. (iii) Useful in understanding drug-receptor binding and the mechanism of drug action [14–19]. (iv) Useful in studying the thermodynamics and pharmacodynamics of drug molecules [20,21]. (v) Obtains quantitative estimates of drugs in pure form or in pharmaceutical preparations that are cheaper, simpler, rapid, accurate and more efficient than the methods of drug determination described in the literature. [22–26]. (vi) Plays important roles in many biological fields such as DNA-binding, antibacterial, antifungal and insecticidal [27–30]. (vii) Several CT complexes of drugs exhibit antimicrobial activities against Gram-positive and Gram-negative bacteria and fungi [22,23,26,31–36,39–41,43–49]. (viii) Removes and utilizes discarded drugs from the environment [50].

We thoroughly study the CT interaction of different medically important drugs with a TCNE acceptor to learn more about the behavior of this interaction, to shed new light on the optical response of these drugs towards TCNE, and to provide basic data that can be used for the detection or determination of these drugs in the environment by spectrophtometry. We found that, some drugs reacted *via* 1:1 M ratio, other reacted *via* 1:2 M ratio. Because of the large data, we divided the investigation into two parts. In this part, we represented the spectrophotometric and thermodynamic data for the 1:1 reaction of eight drugs with TCNE.

1.2. Drugs used in this study

Table 1 shows the chemical structure, abbreviation, and molecular weight of the drugs used in this study. Herein we give a short summary of each one.

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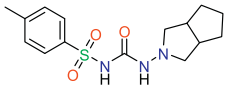
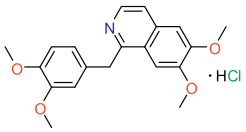
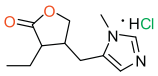
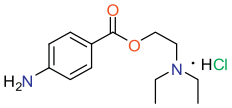
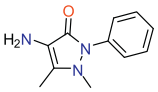
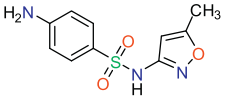
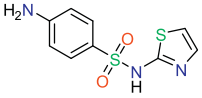
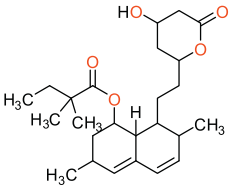
Table 1
Chemical structure, abbreviation, and molecular weight of the drugs used in this study.

Drug	Abbreviation	Chemical structure	MW (g/mol)
Gliclazide	*Drug 1*		323.41
Papaverine HCl	*Drug 2*		375.86
Pilocarpine HCl	*Drug 3*		244.72
Procaine HCl	*Drug 4*		272.78
4-Aminoantipyrine	*Drug 5*		203.24
Sulfamethoxazole	*Drug 6*		253.28
Sulfathiazole	*Drug 7*		255.32
Simvastatin	*Drug 8*		418.57

1.2.1. Gliclazide (Drug 1)

It is classified as a second generation sulfonylurea oral antidiabetic drug. It is used in the treatment of patients with type 2 diabetes through controlling blood glucose [51–56]. It acts mainly on pancreatic sulfonylurea receptors (SURs), at the surface of β-cells, by increasing the secretion of insulin [57].

1.2.2. Papaverine (Drug 2)

It is an opium alkaloid that relaxes many types of smooth muscles [58]. It is used as an antispasmodic drug and as a cerebral and coronary vasodilator for relieving renal colics and penile impotence [59–62]. Due to its vasodilating activity, it increases the cerebral blood flow and decreases cerebrovascular resistance [63,64]. Currently, it is approved for treating spasms of the gastrointestinal tract, bile ducts and ureter [65].

1.2.3. Pilocarpine (Drug 3)

It is a naturally occurring compound derived from the leaves of the South American shrub *Pilocarpus jaborandi*. It is a parasympathomimetic agent that functions primarily as a muscarinic agonist with mild beta-adrenergic activity. This alkaloid causes pharmacologic stimulation of exocrine glands in humans, resulting in diaphoresis, salivation, lacrimation, and gastric and pancreatic secretion. Topical ophthalmic pilocarpine has long been used to treat glaucoma [66,67].

1.2.4. Procaine (Drug 4)

It is a synthetic local anesthetic drug of the amino ester family that produces a reversible loss of sensation by diminishing the conduction of sensory nerve impulses [68,69]. It has long been employed as a pharmacological agent in the life sciences and in clinical therapeutic studies. This drug is primarily used to reduce pain from the intramuscular injection of penicillin, and it is also used in dentistry [70–72].

1.2.5. 4-Aminoantipyrine (Drug 5)

It is a metabolite of aminophenazone and is an aromatic substance with analgesic, antipyretic, antiphlogistic and anti-inflammatory properties [73–75]. It is widely used in pharmacological [76], clinical [77], biological, biochemical [78] and analytical applications [79], as well as in environmental monitoring. It can reduce blood flow [80] and form stable complexes with heme [81]; moreover, it has an obvious denaturing effect on bovine hemoglobin [82].

1.2.6. Sulfamethoxazole (Drug 6) and sulfathiazole (Drug 7)

Sulfonamides are synthetic antibiotics derived from sulfanilic acid; they constitute an important and one of the older groups of *anti*-microbial compounds [83–85]. This family includes a broad-spectrum of bacteriostatics used against most Gram-positive and many Gram-negative microorganisms and protozoa [86,87]. Sulfamethoxazole is the most widely prescribed antibiotic in developed countries because it is cheap and effective [88,89], while sulfathiazole is widely used in veterinary practices for the treatment of various bacterial infections [84].

1.2.7. Simvastatin (Drug 8)

It is an antilipemic drug of the statin class, which acts to reduce LDL cholesterol levels by promoting inhibition of HMG-CoA reductase and consequently, lowers the risk of atherosclerosis and myocardial infarction [90–92]. Recently, its therapeutic effects beyond plasma cholesterol lowering in cell regeneration, have been utilized in areas such as the induction of bone tissue regeneration and anti-inflammatory activity on skin and fracture healing [93–96].

2. Experimental details

2.1. Materials and equipment

2.1.1. Materials

All chemicals used were of analytical grade with highest purity available and were all used as received. Pharmaceutical compounds [papaverine hydrochloride ($C_{20}H_{21}NO_4 \cdot HCl$), pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$), procaine hydrochloride ($C_{13}H_{20}N_2O_2 \cdot HCl$), simvastatin ($C_{25}H_{38}O_5$) and tetracyanoethylene (TCNE)] were supplied by Sigma-Aldrich Chemical Company. Other pharmaceutical compounds [Gliclazide ($C_{15}H_{21}N_3O_3S$), 4-aminoantipyrine ($C_{11}H_{13}N_3O$), sulfamethoxazole ($C_{10}H_{11}N_3O_3S$), and sulfathiazole ($C_9H_9N_3O_2S_2$)] were obtained from Fluka. HPLC-grade acetonitrile (MeCN) was purchased from Merck Company and used without any further purification.

2.1.2. Equipment

The electronic absorption spectra were recorded over a wavelength range of 320–800 nm using a Genesys 10S UV–Vis spectrophotometer (USA) with quartz cells (1.0 cm). The infrared (IR) spectra of the solid products (as KBr discs) were acquired at room temperature using a Shimadzu FT-IR spectrophotometer (Japan) over the range of 4000–400 cm^{-1}. Elemental analyses of the carbon, hydrogen and nitrogen contents were analyzed with a Perkin-Elmer 2400 series CHN microanalyzer (USA).

2.2. Preparation of standards

Stock standard solutions used for the spectrophotometric measurements were prepared at a concentration of 5.0×10^{-3} M by dissolving appropriate amounts of each drug and the TCNE acceptor in a 100 mL volumetric flask using MeCN solvent. The working solutions were prepared by mixing appropriate volumes of the drugs or the TCNE acceptor