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Charge transfer complex of some nervous and brain drugs – Part 1: Synthesis, spectroscopic, analytical and biological studies on the reaction between haloperidol antipsychotic drugs with π-acceptors

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HIGHLIGHTS

- Synthesis of charge transfer complex of some nervous and brain drugs.
- Spectroscopic studies on the reaction between haloperidol with π-acceptors.
- The stoichiometry of these complexes was found to be 1:1 M ratio.
- These complexes were also tested for their antimicrobial activity against six different microorganisms.

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ABSTRACT

Donor–acceptor interactions between the electron donor haloperidol (HPL) and π-acceptors like 7,7,8,8-tetracyanoquinodimethane (TCNQ) and picric acid (PA) have been studied spectrophotometrically in CH_3OH solvent. The donor–acceptor (charge transfer complexes) were discussed in terms of formation constant (K_{CT}), molar extinction coefficient (ε_{CT}), standard free energy (ΔG^o), oscillator strength (f), transition dipole moment (μ), resonance energy (R_N) and ionization potential (I_D). The stoichiometry of these complexes was found to be 1:1 M ratio and having the formulas [(HPL)(TCNQ)] and [(HPL)(PA)], respectively. The charge transfer interaction was successfully applied to determine of HPL drug using mentioned common π-acceptors also, the results obtained herein are satisfactory for estimation of HPL compound in the pharmaceutical form. The formed solid charge-transfer complexes were also isolated and characterized using elemental analysis, conductivity, (infrared, Raman, and ^{1}HNMR) spectra and X-ray powder diffraction (XRD). The experimental data of elemental analyses are in agreement with calculated data. The infrared spectra of both HPL complexes are confirming the participation of —OH of 4-hydroxy-1-piperidyl moiety in the donor–acceptor chelation. The morphological surface of the resulted charge transfer complexes were investigated using scanning electron microscopy (SEM). The thermogravimetric analysis (TG/DTG) and differential scanning calorimetry (DSC) techniques were performed to give knowledge about the thermal stability behavior of the synthesized charge transfer complexes. Thermodynamic parameters were computed from the thermal decomposition data. These complexes were also tested for their antimicrobial activity against six different microorganisms, and the results were compared with the parent drug.

1. Introduction

Haloperidol (Scheme 1) is a typical antipsychotic. It is in the butyrophenone class of antipsychotic medications and has pharmacological effects similar to the phenothiazines [1]. Haloperidol is an older antipsychotic used in the treatment of schizophrenia [2] and in the treatment of acute psychotic states and delirium. A long-acting decanoate ester is used as an injection given every 4 weeks to people with schizophrenia or related illnesses who have a poor compliance with medication and suffer frequent relapses of illness, or to overcome the drawbacks inherent to its orally administered counterpart that burst dosage increases risk or intensity of side effects. In some countries, injections of antipsychotics such as

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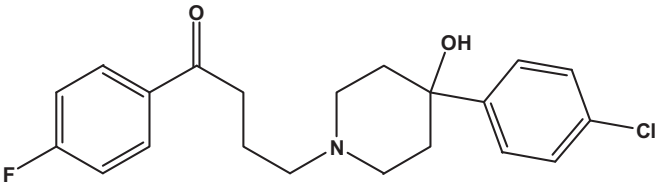
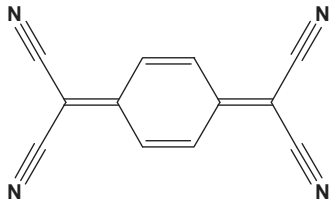
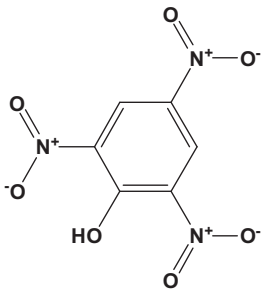


HPL



TCNQ



PA

Scheme 1. Haloperidol drug (HPL); IUPAC name 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidyl]-1-(4-fluorophenyl)-butan-1-one, acceptors; 7,7,8,8-tetracyanoquinodi methane (TCNQ) and picric acid (PA).

Table 1
Analytical and physical data for haloperidol (HPL) charge transfer complexes.

Compound Empirical formula (M. Wt.)	Color Before ppt	Color After ppt	Λm (Ω^{-1} cm^{-1} mol^{-1})	Elemental analysis (%) Found (Calcd.)			Yield (%)
				C	H	N	
HPL 375.86	White	White	10	67.11	6.17	3.73	–
[(HPL)(PA)]	Yellow	Yellow	45	53.39	4.21	9.12	89
(604.968)				(53.60)	(4.33)	(9.26)	
[(HPL)(TCNQ)]	Olive	Green	53	68.43	4.49	11.98	93
(579.043)	Green			(68.45)	(4.53)	(12.09)	

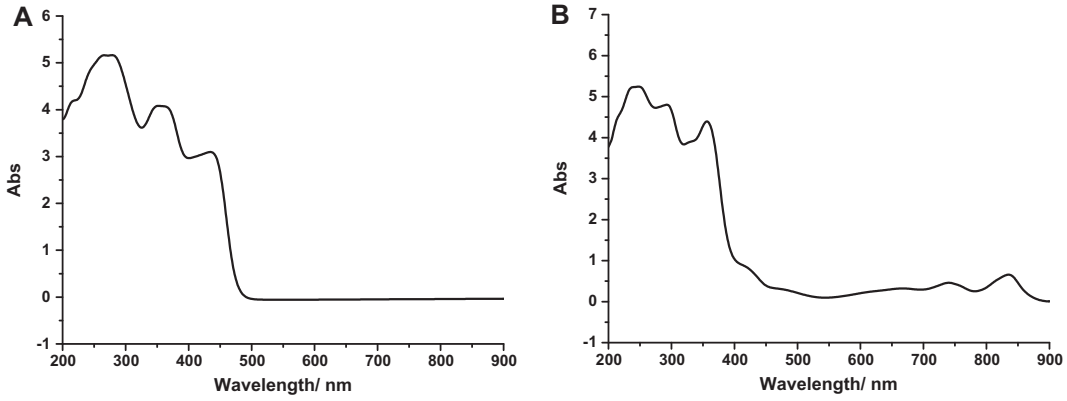


Fig. 1. Electronic absorption spectra of (A): [(HPL)(PA)] and [(HPL)(TCNQ)] charge transfer complexes in methanol solvent.

haloperidol can be ordered by a court at the request of a psychiatrist.

Donor acceptor complexation is an important phenomenon in biochemical and bioelectrochemical energy transfer process [3]. Charge transfer interactions between electron donors and acceptors are generally associated with the formation of intensely colored CT complexes which absorb radiation in the visible region [4]. Molecular complexation and structural recognition are important processes in biological systems; for example, drug action, enzyme catalysis, and ion transfers through lipophilic membranes all involve complexation [5]. Mulliken suggested that the formation of molecular complexes from two aromatic molecules can arise from the transfer of an electron from a π-molecular orbital of a Lewis base to vacant π-molecular orbital of a Lewis acid, with resonance between this dative structure and the no-band structure stabilizing the complex [6]. Mulliken also noted the possibility of complex for-