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Quick and Simple Formation of Charge Transfer Complexes of Brain and Nerves Phenytoin Drug with Different π–acceptors: Chemical and Biological Studies

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Charge transfer complexes formed from the chemical reactions between phenytoin drug (phen) as a n-electron donor and π-acceptors like 2,6-dichloroquinone-4-chloroimide (DCQ), 2,6-dibromoquinone-4-chloroimide (DBQ) and *N*-bromosuccinimide (NBS) were spectrophotometrically discussed and synthesized in solid form. Spectroscopic and physical data such as 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_p) were estimated in methanol at 25 ^{o}C. Upon the elemental analysis and photometric titrations the CT-complexes were formed indicated the formation of 1:2 charge-transfer complexes. The charge-transfer interactions were interpretative according to the formation of dative ion pairs [phen $^{\cdot +}$, $A^{\cdot -}$], where A is acceptor. All of the resulting charge transfer complexes were isolated in solid colored form and the complexes were discussed using infrared and proton NMR spectra. The surface morphology of the three phen complexes was scanned by scanning electron microscopy (SEM). In addition, the forned synthesized complexes was tested for antibacterial and antifungal activities against different strains of microorganism by disc diffusion method. The different antimicrobial activities depend on sanitized chemical structure and microorganism strains were recorded.

Keywords: Phenytoin; charge transfer complexes; DCQ; DBQ; NBS.

1. INTRODUCTION

Phenytoin (phen; Fig. 1) is a hydantoin-derivative anticonvulsant drug used primarily in the management of complex partial seizures and generalized tonic-clonic seizures. Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage-gated sodium channels [1].

Additionally, phenytoin is a class 1b antiarrhythmic that can be used to treat cardiac arrhythmias when conventional options have failed or after cardiac glycoside intoxication [2]. Charge-transfer complexes are known to take part in many chemical reactions like addition, substitution and condensation [3, 4]. These complexes have great attention for non-linear optical materials and electrical conductivities [5-8]. Electron donor-acceptor CT- interaction is also important in the field of drug-receptor binding mechanism [9], in solar energy storage [10] and in surface chemistry [11] as well as in many biological fields [12].

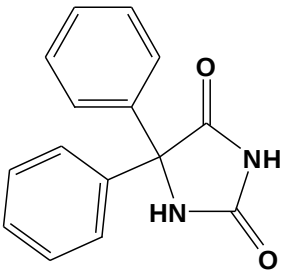
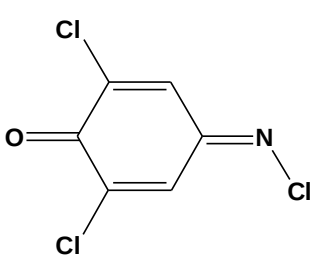
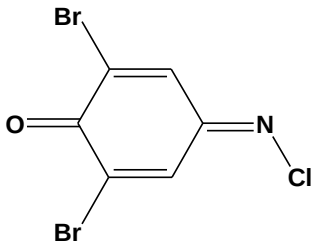


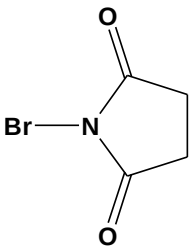
Figure 1. Structure of phenytoin drug



2,6-dichloroquinone-4-chloroimide
(DCQ)



2,6-dibromoquinone-4-chloroimide
(DBQ)



N-bromosuccinimide
(NBS)

Figure 2. Structures of 2,6-dichloroquinone-4-chloroimide (DCQ), 2,6-dibromoquinone-4-chloroimide (DBQ) and *N*-bromosuccinimide (NBS) as π-acceptors

On the other hand, the charge transfer reactions of certain π- acceptors have successfully utilized in pharmaceutical analysis [13]. For these wide applications extensive studies on CT-complexes of π- acceptors have been performed [14]. Charge-transfer complexes of organic species are intensively studied because of their special type of interaction, which is accompanied by transfer of an electron from the donor to the acceptor [15, 16]. Also, protonation of the donor from acidic acceptors are generally rout for the formation of ion pair adducts [17-19]. The π–acceptors have numerous

applications as analytical reagents that, they have been used for the spectrophotometric determination of many drugs in pharmaceutical formulations [20-26]. In view of our knowledge, no wide spectroscopic studies have been performed for the interactions between phenytoin drug and different classes of π–acceptors. Uponuiriasd the advantage of electronic spectroscopy technique in terms of simple, low cost, popular and fast properties, this paper describes, the spectrophotometric determination of phenytoin based on the charge transfer interaction between π–acceptors (Fig. 2) and the sp^3 nitrogen atom of secondary amine group of phen as a good n-electron donor to form charge-transfer complexes. Also, no biological studies have been focused on synthesized compounds im present study as antibacterial or antifungal. Inhibition growth zone diameter (mm) against gram positive; gram negative bacteria and different fungal strains were recorded by agar well diffusion method.

2. EXPERIMENTAL

2.1. Materials

Phenytoin was received from Egyptian International Pharmaceutical Industries Company EIPICO. The 2,6-dichloroquinone-4-chloroimide (DCQ), 2,6-dibromoquinone-4-chloroimide (DBQ) and *N*-bromosuccinimide (NBS) were obtained from Aldrich and Fluka Chemical Companies. All chemicals are analytical grade and used without further purification.

2.2. Synthesis of solid phenytoin sodium charge transfer complexes

Three solid phenytoin charge transfer complexes were synthesized as a dark brown, brown, pale yellow colors for the DBQ, DCQ and NBS complexes, respectively, by mixing a (1 mmol, 0.253 gm) of phenytoin drug in 30 mL methanol to 1 mmol of each acceptors in 20 mL methanol solvent. All mixtures were stirred for 45 min at room temperature and the solid products were filtered off, washed with minimum amounts of chloroform and dried under vacuum over anhydrous $CaCl_2$.

i.[(phen)$(DCQ)_2$]
Mol. Wt. = 673.16; Calcd: %C, 48.17; %H, 2.40; %N, 8.32, Found: %C, 48.11; %H, 2.31; %N, 8.21.

ii.[(phen)$(DBQ)_2$]
Mol. Wt. = 850.96; Calcd: %C, 38.11; %H, 1.90; %N, 6.58, Found: %C, 38.03; %H, 1.85; %N, 6.50.

iii.[$(phen^{\cdot+})(NBS^{\cdot-})_2$]
Mol. Wt. = 612.27; Calcd: %C, 45.12; %H, 3.95; %N, 9.15, Found: %C, 45.02; %H, 3.88; %N, 9.07.

2.3. Physical and analytical measurements

The elemental analyses of carbon, hydrogen and nitrogen contents were performed using a Perkin Elmer CHN 2400. The molar conductivities of freshly prepared 1.0×10^{-3} mol/cm^3 dimethylsulfoxide (DMSO) solutions were measured for the dissolved phenytoin charge transfer complexes using Jenway 4010 conductivity meter. The electronic absorption spectra of the resulted charge transfer complexes were recorded in methanol within 900-200 nm range using a Perkin-Elmer Precisely Lambda 25 UV/Vis double beam Spectrometer fitted with a quartz cell of 1.0 cm path length. Infrared spectra within the range of 4000-400 cm^{-1} for the free reactants and the resulted charge transfer complexes were recorded from KBr discs using a Shimadzu FT-IR Spectrometer with 30 scans and 2cm^{-1} resolution. ^{1}H-NMR was recorded as DMSO solutions on a Bruker 600 MHz spectrometer using TMS as the internal standard. Scanning electron microscopy (SEM) images were taken in Joel JSM-6390 equipment with an accelerating voltage of 20 KV.

3. RESULTS AND DISCUSSIONS

Solid samples of the 1:2 charge transfer complexes of phen were prepared by mixing 50 mL methanol solutions of phen (1.0 mM) and either (DCQ, DBQ and NBS) acceptor (2.0 mM). The percentage of each essential element of carbon, hydrogen, and nitrogen for the resulted phenytoin charge transfer complexes are agreement with the photometric titration ratios. The electronic spectra of charge transfer systems of phenytoin donor with the different π-acceptors (DCQ, DBQ and NBS) were scanned and introduced in Fig. 3.

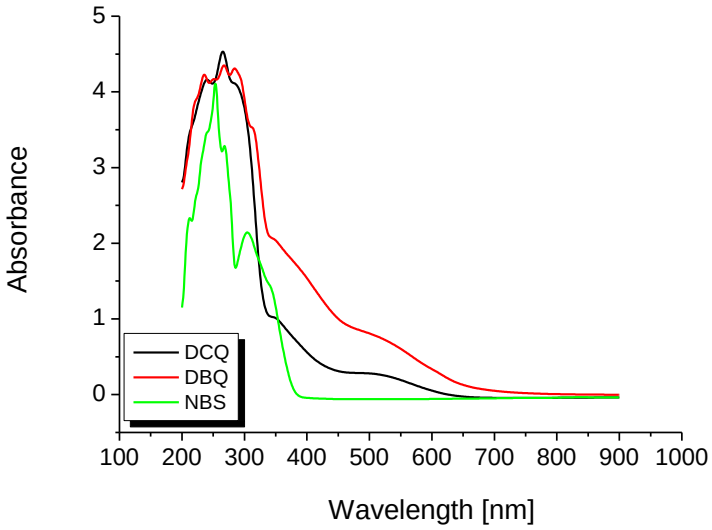


Figure 3. Electronic spectra of phenytoin donor with DCQ, DBQ and NBS charge transfer systems.

Spectrophotometric titrations at 522, 545 and 306 nm were performed for the reactions of phen with DCQ, DBQ and NBS, respectively, using the Jenway 6405 spectrophotometer as follows: A 0.25, 0.50, 0.75, 1.00, 1.50, 2.00, 2.50, 3.00, 3.50 and 4.00 mL aliquot of a standard solution (5.0×10^{-4} M) of

the appropriate acceptors (DCQ, DBQ and NBS) in methanol was added to 1.00 mL of 5.0×10^{-4} M phenytoin also in methanol. The total volume of the mixture was 5 mL. The concentration of phen (C^o_d) in the reaction mixture was thus fixed at 1.0×10^{-4} M while the concentration of π-acceptors (C^o_a) varied from 0.25×10^{-4} M to 4.00×10^{-4} M. These concentrations produce [donor]: [acceptor] ratios from 4:1 to 1:4. The absorbance of each charge transfer complexes was measured and plotted (Fig. 4) as a function with the ratio of (C^o_d): (C^o_d) according to a known method [27]. It was of interest to observe that the solvent has a pronounced effect on the spectral intensities of the formed charge transfer complexes. To study this solvent effect in a quantitative manner, it was necessary to calculate the values of the equilibrium constant, K, the molar absorptivity ε, and the oscillator strength, *f*, of the phen complexes in the respective solvent. The molar ratio of 1:2 has been represented in equation (1) [28].

$$\frac{C_A^{o^2} C_D^o}{A} = \frac{1}{K\varepsilon} + \frac{1}{\varepsilon}.C_A^o\left(4C_D^o + C_A^o\right) \quad \text{..... (1)}$$

Where $C_A^{o^2}$ and C_D^o are the initial concentration of the π-acceptor (DCQ, DBQ and NBS) and donor (phen), respectively, and A is the absorbance of the detected charge transfer bands. The data obtained $C_D^o, C_A^{o^2}$, $C_A^o\left(4C_D^o + C_A^o\right)$ and $(C_A^{o^2}.C_D^o)$/A in methanol were calculated. By plotting $(C_A^{o^2}.C_D^o)$/A values vs $C_A^o\left(4C_D^o + C_A^o\right)$, straight lines (Fig. 5) were obtained with a slope of 1/ε and an intercept of 1/Kε.

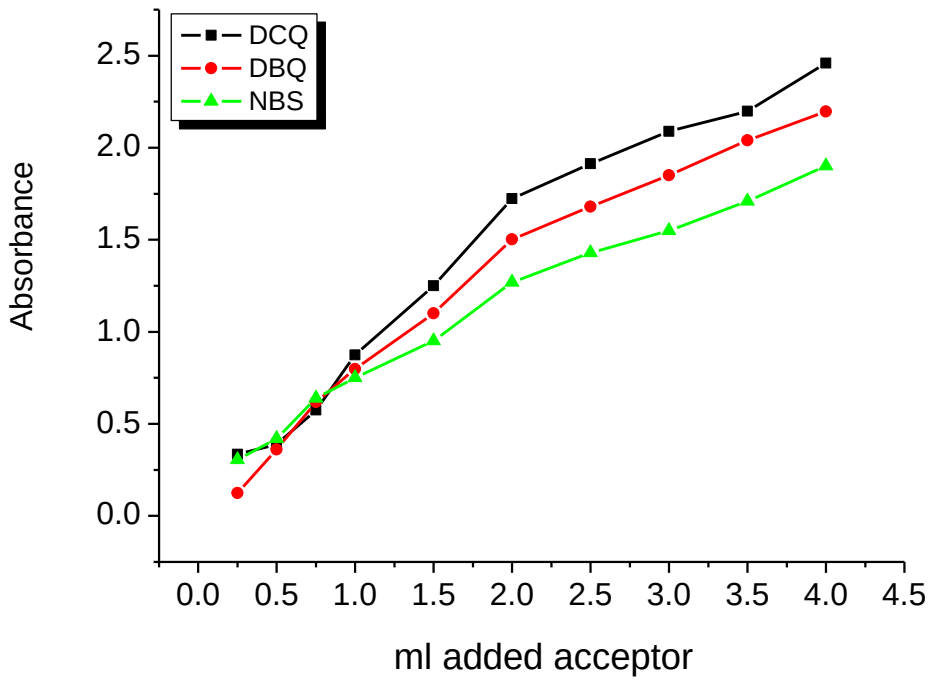


Figure 4. Molar ratio curve of phenytoin with DCQ, DBQ and NBS charge transfer systems.

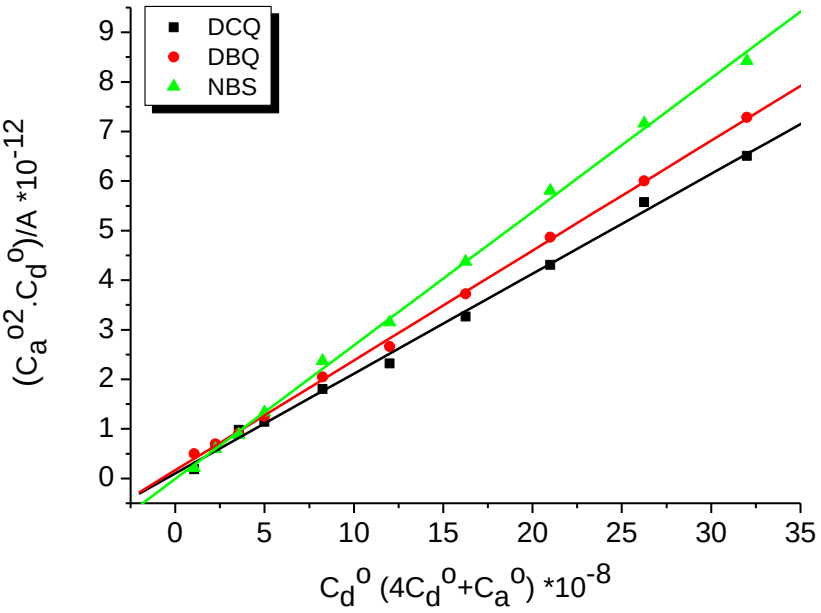


Figure 5. Plot of $(C_A^{o^2}.C_D^{o})$/A values vs $C_A^{o}\left(4C_D^{o}+C_A^{o}\right)$ for the phenytoin with DCQ, DBQ and NBS charge transfer systems.

The physical spectroscopic data like 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_p) were calculated in methanol solvent at 25 ^{o}C, and the different acceptors were found to have a pronounced effect towards the interaction with phenytoin drug donor. These calculations can be summarized as follows;

3.1. Oscillator strength

The oscillator strength *f* was obtained from the approximate formula [29].

$f = (4.319 \times 10^{-9})\ \varepsilon_{max}\ .\ \nu_{1/2}$ …. (2)

Where $\nu_{1/2}$ is the band-width for half-intensity in cm^{-1} and ε_{max} is the maximum extinction coefficient of the CT-band. The oscillator strength values are given in Table 1. The data resulted reveals several items. i) The [(phen)$(A)_2$] (where A= DCQ, DBQ and NBS) charge transfer systems show high values of both formation constant (*K*) and molar absorptivity (ε). This high value of (*K*) reflects the high stability of the phenytoin charge transfer complexes as a result of the expected high rich donation of the phen which contains two nitrogen atoms, ii) the different values of the oscillator strength, *f*, increases with increasing in the dielectric constant (*D*) of the solvent. This result could be explained on the basis of competitive solvent interactions with the acceptors [30, 31].

3.2. Transition dipole moment

The transition dipole moment (μ) of the phenytoin drug charge transfer complexes, Table 1, have been calculated from the equ. 3 [32];

μ (Debye) $= 0.0958[\varepsilon_{max}\ \nu_{1/2}\ /\ \nu_{max}]^{1/2}$ ..... (3)

where $\nu_{1/2}$ is the half bandwidth of absorbance, ε_{max} and ν_{max} the extinction coefficient and wavenumber at maximum absorption peak of the CT complex, respectively. The transition dipole moment is useful for determining if transitions are allowed, that the transition from a bonding π orbital to an antibonding π^* orbital is allowed because the integral defining the transition dipole moment is nonzero.

3.3. Ionization potential

The ionization potential (I_p) of the phenytoin charge transfer complexes were calculated using empirical equation derived by Aloisi and Piganatro equ. (4) [33, 34];

$I_p\ (ev) = 5.76 + 1.53\times10^{-4}\ \nu_{CT}$ ..... (4)

Where, ν_{CT} is the wavenumber in cm^{-1} corresponding to the charge transfer band formed from the interaction between donor and acceptor. The electron donating power of a donor molecule is measured by its ionization potential which is the energy required to remove an electron from the highest occupied molecular orbital.

3.4. Energy of the charge-transfer complexes

The energy of the charge-transfer complexes E_{CT} of the phenytoin charge transfer complexes is calculated using the equ. 5[35];

$E_{CT} = (h\nu_{CT}) = 1243.667 / \lambda_{CT}\ (nm)$ ……(5)

Where, λ_{CT} is the wavelength of the complexation band. The values of E_{CT} are listed in Table 1, which show that the lower the ionization potential of the electron donor, the smaller is the transition energy of the charge transfer band.

3.5. Resonance energy

Determination of resonance energy *(R_N)* [36] theoretically derived from (equ. 6)*;*

$\varepsilon_{max} = 7.7 \times 10^{-4} / [h\nu_{CT}/ [R_N] - 3.5]$ ..... (6)

Where ε_{max} is the molar absorptivity of the phenytoin charge transfer complexes at maximum CT band, ν_{CT} is the frequency of the CT peak and R_N is the resonance energy of the complex in the ground state, which, obviously is a contributing factor to the stability constant of the complex (a ground state property). The values of R_N for the phenytoin charge transfer complexes under study have been given in Table 1.

3.6. Free energy

The standard free energy changes of complexation (ΔG^o) were calculated from the formation constants by the following equ. (7) [37];

$\Delta G^o = - 2.303\ RT \log K_{CT}$ …. (7)

Where ΔG^o is the free energy change of the phenytoin charge transfer complexes (KJ mol^{-1}), R is the gas constant (8.314 J mol^{-1} K), T is the temperature in Kelvin degrees (273 + ^oC) and K_{CT} is the formation constant of the complexes ($lmol^{-1}$) in different solvents at room temperature.

Table 1. Physical spectroscopic data of phenytoin with DCQ, DBQ and NBS charge transfer systems.

Complex	λ_{max} (nm)	E_{CT} (eV)	K ($l.mol^{-1}$)	ε_{max} ($l.mol^{-1}.cm^{-1}$)	*f*	μ	I_p	R_N	$\Delta G^o(25^oC)$ $Jmol^{-1}$
[(phen)$(DCQ)_2$]	522	2.38	19600	$497*10^6$	$0.21*10^6$	0.21	8.69	0.681	-24490
[(phen)$(DBQ)_2$]	545	2.28	13400	$451*10^6$	$0.19*10^6$	0.47	8.57	0.652	-23549
[(phen)$(NBS)_2$]	306	4.06	33370	$371*10^6$	$0.160*10^6$	0.32	10.76	1.16	-31515

The equilibrium constants are strongly dependent on the nature of the used acceptor including the type of electron withdrawing substituents to it such as halo groups. For example, Table 1, the value of equilibrium constant for [(phen)$(NBS)_2$] is highest value than both [(phen)$(DCQ)_2$] and [(phen)$(DBQ)_2$] complexes in methanol solvent. This value is about twice higher than the values of equilibrium constant for the complexes [(phen)$(DCQ)_2$] and [(phen)$(DBQ)_2$], respectively, reflecting the relatively higher electron acceptance ability for NBS. The number of donating atoms available is another important factor that affects the stability of phenytoin complexes. Since in the process of molecular complexation, it is reasonably assumed that the charge density is donated from the donor to acceptor, the increased number of donating atoms in the ring is expected to increase the donor-acceptor interaction in solution. The effective overlapping of donor-acceptor orbitals involves the proper spatial positions of donor and acceptor molecules. This also needs specific conformation of donor. If the conformation of donor in the complexes form differs significantly from, it's most stable conformation in the Free State. During complexation, some energy will consume for the conversion of most stable conformation of free donor to a conformation which is suitable for complex formation. This will act as a destabiliser factor in the whole process. Among the donor studied, phen has the most rigid structure. So, the variation of its conformation involves energy consumption. Based on this property, the observation of least stability for [(phen)$(DBQ)_2$] (Table 1) is not unexpected. The conductance as a function of [Acceptor]/[phen] mole ratios was measured and the results are shown that there is slightly increase of conductance upon acceptor (DCQ, DBQ and NBS) addition thus, it can be concluded that the complexes are completely nonionic structures except for [$(phen^{\cdot+})(NBS^{\cdot-})_2$ complex has an ion radical form [17-19].

Infrared spectra of phenytoin and their 1:2 [(phen)$(DCQ)_2$], [(phen)$(DBQ)_2$] and [(phen)$(NBS)_2$] charge transfer complexes are compared and interpretative in Table 2. The bands

generally show some shifted upon complexation concerning to the stretching vibrations and intensities of the carbonyl group (acceptor), and N-H (donor) (where X= Cl or Br).

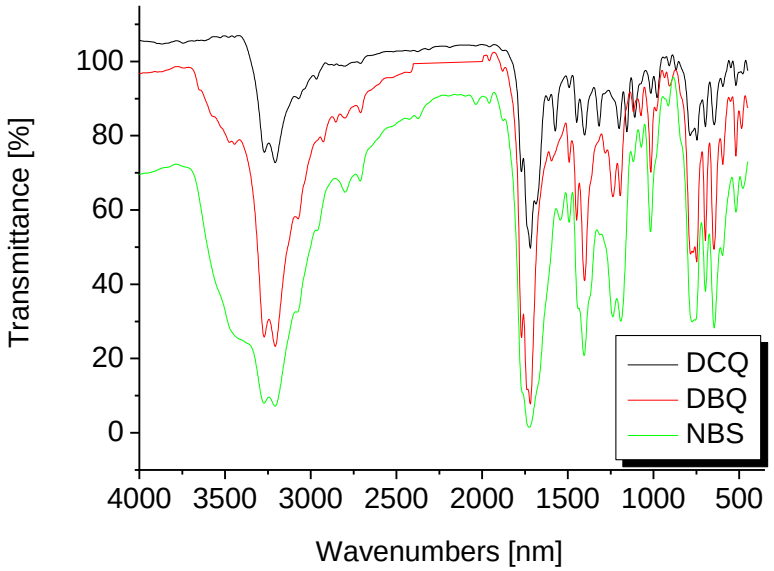
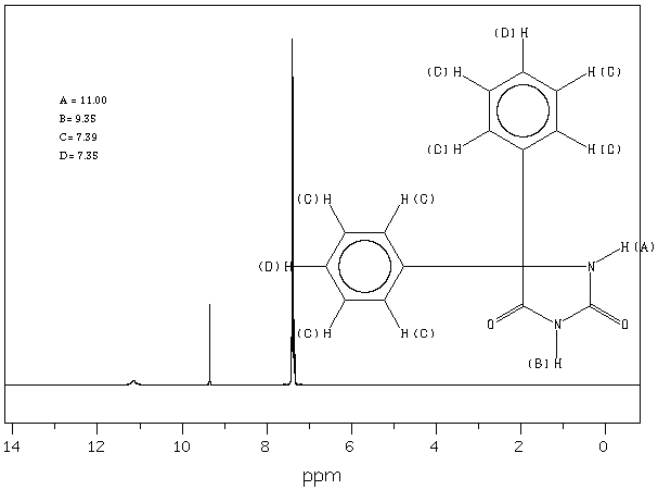


Figure 6. Infrared spectra of DCQ, DBQ and NBS charge transfer complexes

Table 2. Characteristic infrared frequencies (cm^{-1}) and tentative assignments of DCQ, DBQ, NBS and their phenytoin charge transfer complexes

DCQ	DBQ	NBS	phen	[(phen)(acceptor)$_2$]			Assignments[(b)]
				DCQ	DBQ	NBS	
3079 3052 2954 2925 2869 2854	3074	2973 2950 2939 2927	3277 3208 3069	3270 3210 3073 2974	3270 3209 3073 2920	3278 3209 3080	ν(C-H) ν(N-H)
1673	1678	1716	1774 1742 1722	1773 1720	1773 1720	1735	ν(C=O)
1618 1573	1640 1605	--	1699	1576	1590	1553	ν(C=C)
1510 1464	1566 1547 1509	1426 1414	1496 1449	1591 1446 1408	1491 1453	1491	δ(CH) deformation
1376	1342	1311	1403	1317	1401	1408	ν(C-N)
1366 1305 1285 1274 1162 1044 917 898	1301 1270 1143 1013 1002 902 869	1238 1197 1167 1157 1007 965	1287 1242 1198 1118 1106 1032 976 788	1210 1157 1103 1020 906 785 739	1241 1195 1111 1074 1020 906 777	1248 1195 1126 1081 1020 914 777	ν(C-O) ν(C-C) ν(C-X) CH-out of plane



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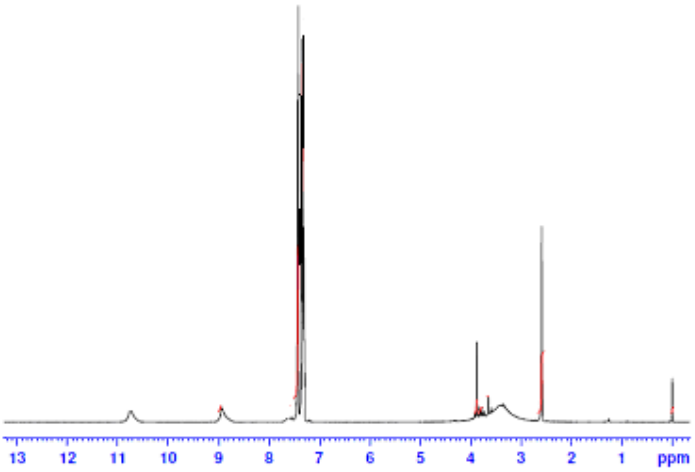

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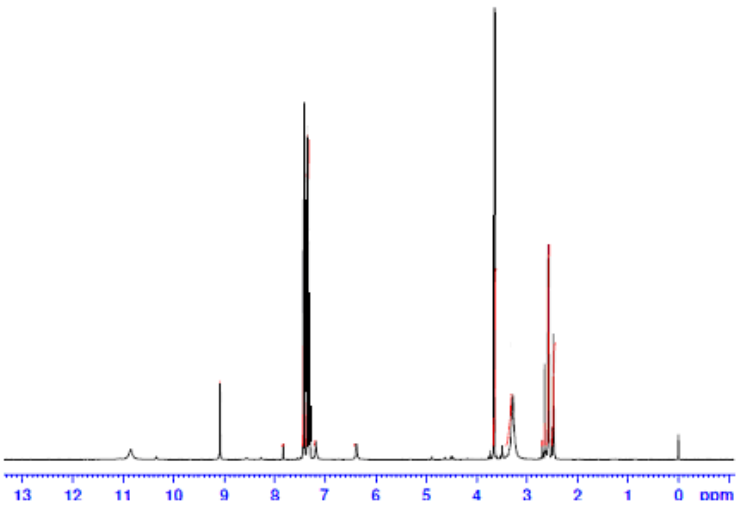
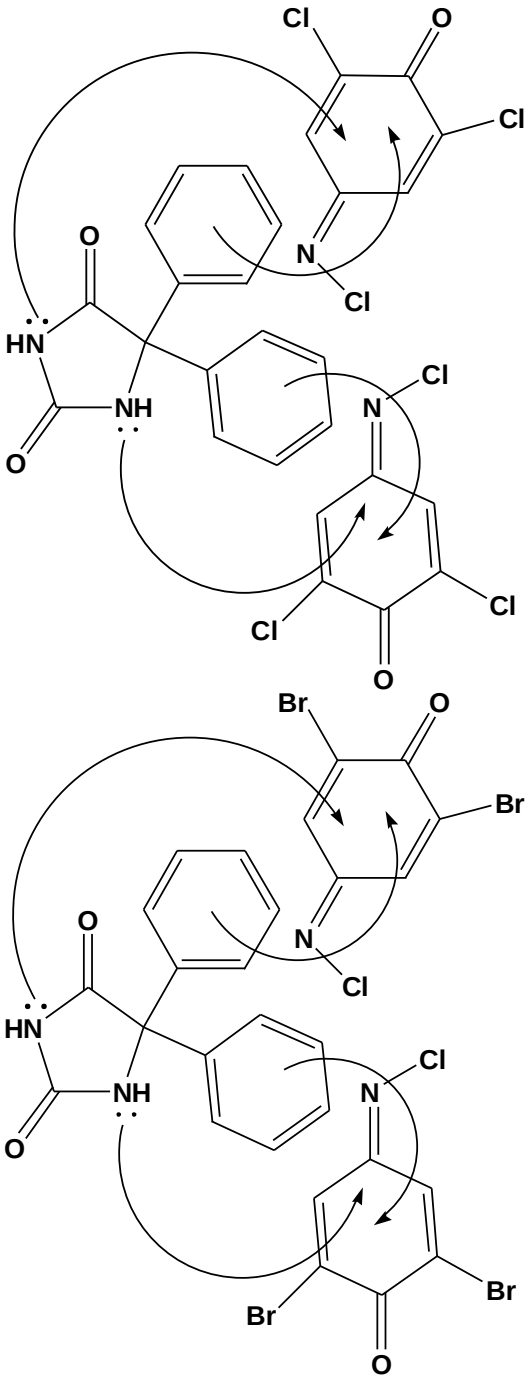
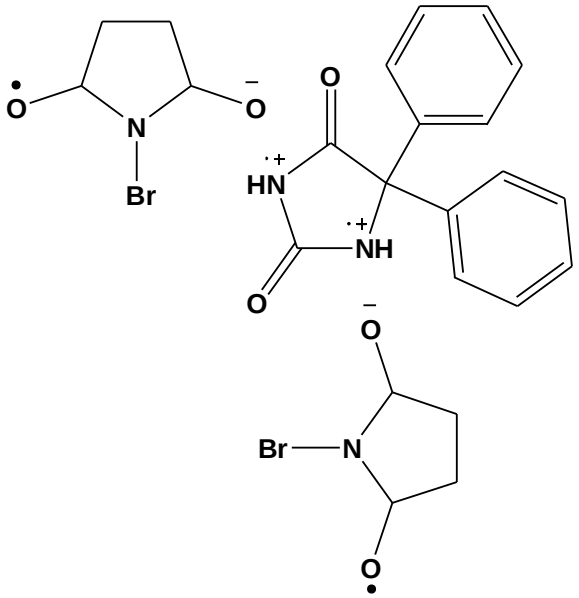


C

Figure 7. ^{1}H-NMR spectra of a: standard phenytoin donor, b: $[(phen)(DCQ)_2]$ and c: $[(phen^{\cdot+})(NBS^{\cdot-})_2]$ charge transfer complexes.

The proton NMR spectra of the phenytoin free donor drug phen and their charge transfer complexes of DCQ and NBS (Fig. 7) were recorded in DMSO-d_6 and chloroform mixed solvent using tetramethylsilane (TMS) as internal standard. The chemical shifts (δ) of the different types of protons of the ligand phen and their charge transfer complexes are discussed and refereed the essential peaks of phen donor in Fig. 7a.



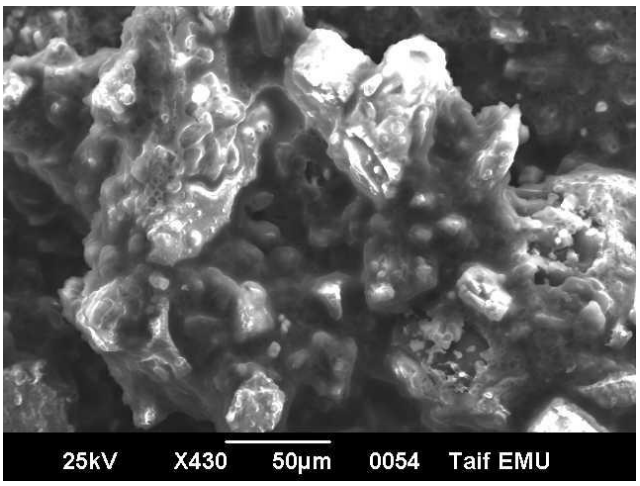


Formula I: Suggested structures of [(phen)(DCQ)$_2$], [(phen)(DBQ)$_2$] and [(phen$\cdot^+$)(NBS$\cdot^-$)$_2$] charge transfer complexes.

In details the chemical shifts of different kinds of protons in phen drug can be justified in Fig. 7a. Both the –NH signals of imidazolidine-2,4-dione moiety for proton in position <A> and <B> (Fig. 7a) found at 11.00 and 9.35 ppm, respectively in the spectrum of the free phenytoin donor is completely downfield in the spectra of both DCQ and NBS complexes, this support the sharing of the two –NH groups of (phen) in charge transfer chelation with aromatic rings and carbonyl groups for DCQ and NBS for acceptors via three types of transitions as n—π*, π—π* and radical anions. In both [(phen)(DCQ)$_2$] and [(phen$\cdot^+$)(NBS$\cdot^-$)$_2$] complexes, the proton NMR spectrum showed signals at (10.80, 9.03, 7.20-7.60) ppm and (10.90, 9.10, 7.20-7.90, 2.4-2.7) ppm are actually shifted lower field due to the intermolecular charge transfer complexes with different transitions via lone pair of electrons on both nitrogen atoms of imidazolidine-2,4-dione ring and the center of accepted groups in the DCQ and NBS acceptors.

Accordingly, the n—π*, π—π* and radical anions between the phen donor and the (DCQ, DBQ and NBS) acceptors can be designed as Formula I.

Microstructure and morphology of the synthesized charge transfer complexes were scanned by electronic microscopy (SEM) and the recorded images are shown in the Fig. 8. The electron micrograph shows that morphology of the different phenytoin charge transfer complexes depend on the acceptor present, due to the different chemical structure of the adducts produced. The uniformity and similarity between the particles forms of synthesized phenytoin charge transfer complexes indicate that the existence of morphological phases of DCQ, DBQ and NBS complexes have a homogeneous matrix. A coral reefs shape (Fig. 8a) is observed in case of the [(phen)(DCQ)$_2$] with the particle size 50 μm. The [(phen)(DBQ)$_2$] charge transfer complex has a different particle sizes like stones (Fig. 8b). A homogeneous phase formation of [(phen)(NBS)$_2$] complex has the rectangular wooden panels morphologies in the form of a dispersed with particle size 20 μm is exhibited in Fig. 8c.



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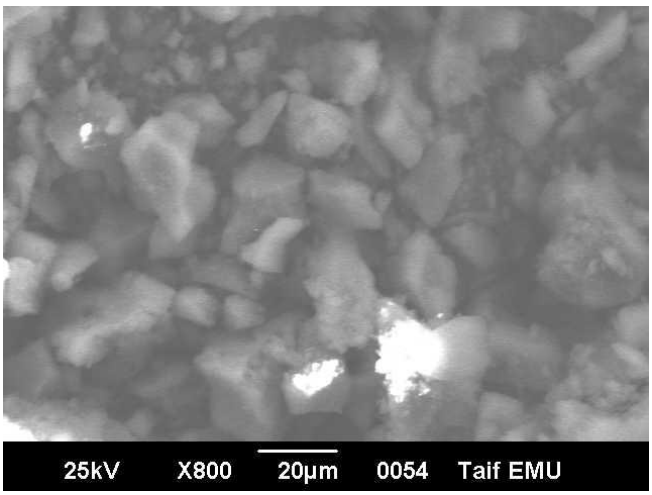

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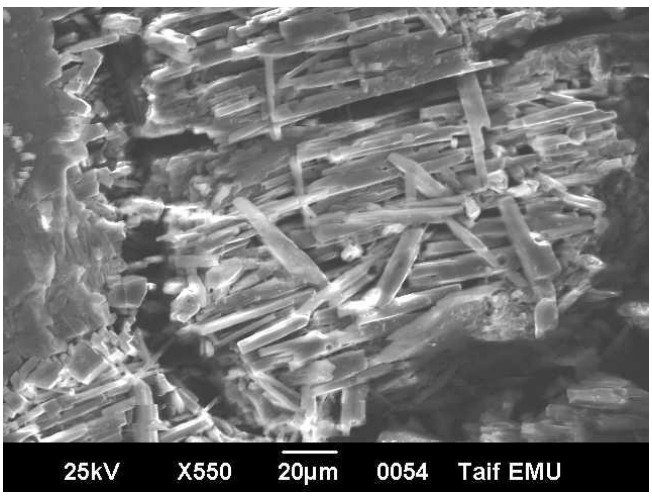

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Figure 8. SEM images of a: [(phen)$(DCQ)_2$], b: [(phen)$(DBQ)_2$] and c: [$(phen^{\cdot+})(NBS^{\cdot-})_2$] charge transfer complexes.

3.7. Biological experiments

Antimicrobial activity of the tested samples was determined using a Kir Bauer disc diffusion method [38]. Briefly, 100 µl of the best bacteria/fungi were grown in 10 mL of fresh media until they reached a count of approximately108 cells/ml for bacteria and 105 cells/ml for fungi. 100 µl of microbial suspension was spread onto agar plates corresponding to the broth in which they were maintained. Isolated colonies of each organism that might be playing a pathogenic role should be selected from primary agar plates and tested for susceptibility by disc diffusion method [39, 40]. National Committee for Clinical Laboratory Standards (NCCLS) recommends Mueller–Hinton agar was used as growing microorganism media. Plates inoculated with filamentous fungi as *Aspergillus niger* ; *Penicillium sp* and *Candida albicans* at 25 ºC for 48hours; Gram (+) bacteria as *Bacillus subtilis; Streptococcus pneumoniae* and *Staphylococcus ureas* ; Gram (⁻) bacteria as E. coli, and *Pseudomonas sp* they were 35–37 ºC for 24–48 hr. and, then the diameters of the inhibition zones were measured in millimetres [38]. Streptomycin (10 mg) and ketoconazole (10 mg) were used as standard antibacterial and antifungal drug respectively.

Antimicrobial activity of charge transfer complexes formed from the chemical reactions between phenytoin drug (phen) as a n-electron donor and π-acceptors like 2,6-dichloroquinone-4-chloroimide (DCQ), 2,6-dibromoquinone-4-chloroimide (DBQ) and *N*-bromosuccinimide (NBS) and streptomycin (10 mg) and ketoconazole (10 mg) as standard antibacterial and antifungal drugs for comparison were evaluated against different strains of bacteria and fungi. The inhibition zone diameter (mm) was recorded in table 3 and illustrated in figure 9. The formed charge transfer complexes showed effective results towards both gram positive; gram negative bacterial and fungal cultures. The complex [(phen)$(DCQ)_2$] was found to be more effective towards all microorganism strains followed by complex [(phen)$(DBQ)_2$], while the complex [(phen)$(NBS)_2$] found to be less effective against all tested strains The antimicrobial activity is probably derived, through the electrostatic attraction between negative charged cell membrane of microorganism and positive charge in formed complexes. The inhibitory effect on microorganisms tested is effected via two possible mechanisms First, is the electrostatic attraction between the negatively charged cell membrane of the microorganisms and the positively charge and second, is the formation of 'pits' in the cell wall of bacteria [41, 42]. Also the results indicated that no zone of inhibition was observed for phenytoin drug (uncharged).

Table 3. Inhibition zones in mm of the phen charge transfer complexes at 1mg/mL.

Compound (mg/ml)	Gram Positive Bacteria			Gram Negative Bacteria		antifungal		
	Bacillus subtilis	*Streptococcus pneumoniae*	*Staphylococcus aureas*	*E.coli*	*Pseudomonas sp.*	*Aspergillus niger*	*Penicillium sp.*	*Candida albicans*
Phen	4	3	3	5	3	3	4	-
[(phen)$(DCQ)_2$]	22	20	24	21	28	20	20	23
[(phen)$(DBQ)_2$]	20	16	20	20	23	17	15	22
[(phen)$(NBS)_2$]	6	7	12	14	14	11	9	11
Streptomycin	18	16	19	22	27	-	-	-
Ketoconazole	-	-	-	-	-	18	21	21

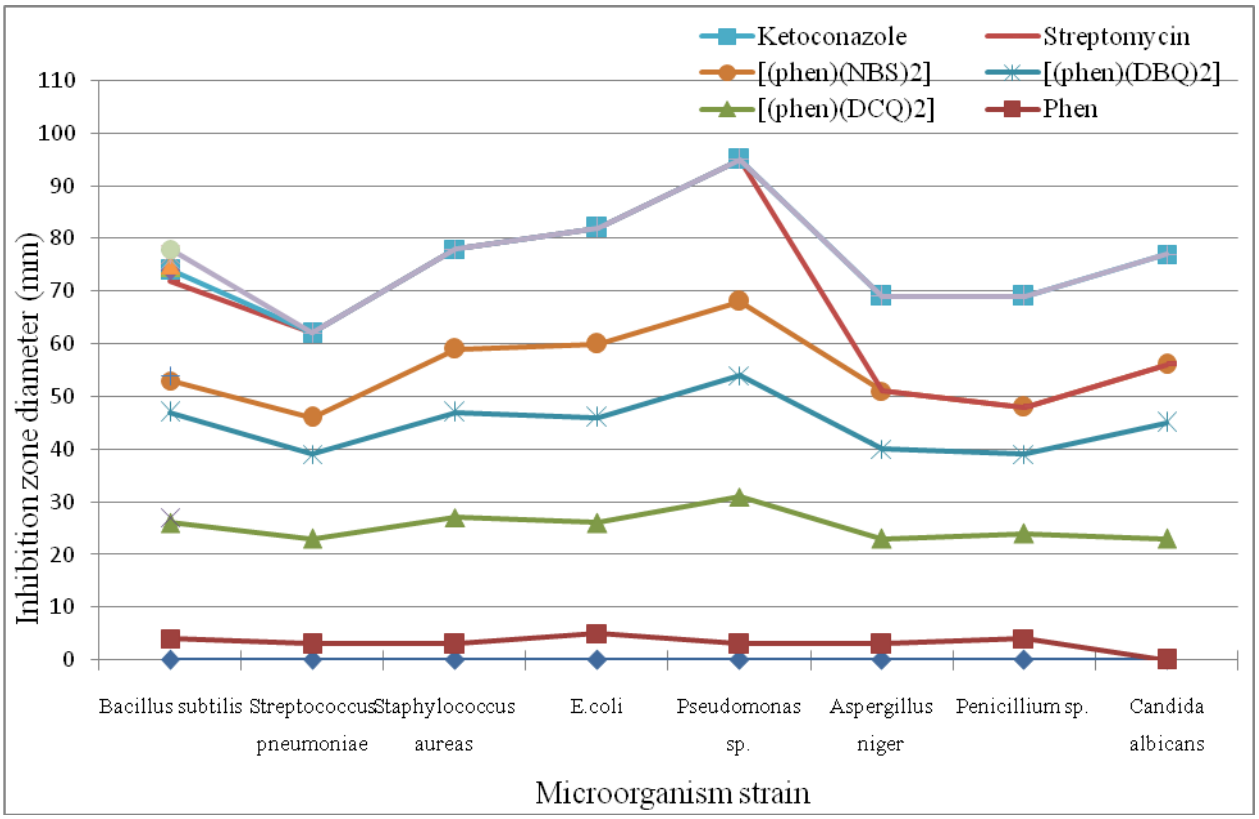

Figure 9. The effect of different microorganism strains on inhibition zone diameter (mm).

The differences observed in the diameter of zone of inhibition may be due to the difference in the susceptibility of different bacteria to the prepared compounds. The differential sensitivity of different microorganism towards formed complexes possibly depends upon their cell structure, physiology, metabolism and their DNA molecules interaction with the charged compounds [43].

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