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Evaluation of biological behavior of New-phenyl ferrocene derivative with DNA using UV/VIS, Cyclic Voltammetry and Molecular Docking techniques

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Abstract

ferrocene derivatives families have attracted the scientist's attention based on all chemical and physical characterizations that have it. In addition, these compounds widely used in different fields in particular biomedical applications. in this investigation have been studied the binding affinity of title compound with DNA using electrochemical and spectroscopic methods and the obtained results have confirmed by a molecular docking study. Despite the years of exhaustive medicinal chemistry studies on the modification of known therapeutic scaffolds, it is becoming increasingly difficult to deliver new leads on this approach and as a result the use of organometallics in biomedical applications has become an active area of research. The use of organometallics as potential therapeutics commenced with the discovery of cisplatin by Rosenberg in 1965 which marked the genesis of bioorganometallic chemistry due to the success of cisplatin against various types of cancer. Furthermore, the incorporation of organometallics into compounds with medicinal applications has resulted in increased efficacy of existing therapeutics . Furthermore, the use of new ferrocene derivatives families as a potential drug has made it possible to avoid the relapse in the long term which is associated with a lot of a number of fatal diseases.

Keywords: (ferrocene, DNA, docking, drug, cancer)

1. Introduction

Deoxyribonucleic acid (DNA) is a significant genetic substance in all living organisms[1]. the molecule of DNA contains vital bodily processes such as gene expression and transcription and also related to mutagenesis and oncogenesis. in a lot of clinical assays, It is well decided that many organic/inorganic anticancer agents bind with DNA and overcame cancer's fatal-effect[2]. More recently, ferrocene is getting a lot of importance in the field of anticancer drug development. Ferrocene has been utilized in laboratory preparation phases of many medicinal drugs[3].

A set of manners are available to study ligand-DNA interaction. UV-visible spectroscopy and cyclic voltammetry are well helped in this intermolecular-investigation[4] .for thirty years ago, The virtual screening of bioactive-compounds for their interaction with biomolecules is becoming popular. Molecular docking is replacing the expensive experimental techniques for the screening of drug potency. In this study, we have used AutoDock computer-software for the virtual binding of the prepared compound with DNA molecule. in an integrated way, the docking results of the computational studies are compared with well-established experimental methods. the structure of ligand is optimized by 3D simulation in Gaussian W03[5].

2. Materials and methods

2.1. Chemical

New-phenyl ferrocene was synthesized according to the literature procedure [6]. This compound gave analytical and spectroscopic data in accordance with the proposed structures (Figure 1).

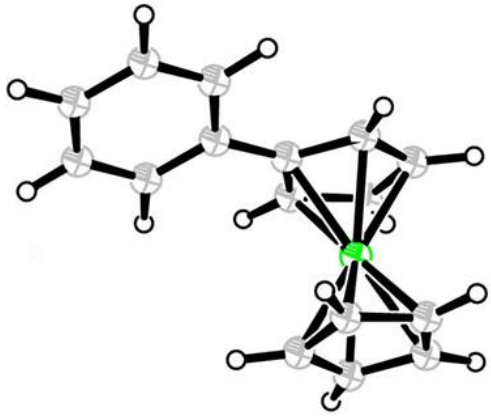

Fig.1. Structure of New-phenyl ferrocene (New-FD)

2.2. DNA extraction

DNA was extracted from chicken blood by Falcon method [21]. Ratio of the absorbance of DNA at λ = 260 nm (A260) and λ = 280 nm (A280) was used to determine the purity of DNA. The obtained ratio of (A260)/(A280) in DNA sample was found to be equal to 1.97, indicating of the purity of DNA [22]. Final DNA concentration was measured by UV absorbance at 260 nm using the molar extinction coefficient of 6600 M−1 cm−1 [23].

2.3. Apparatus and procedures

Voltammetric experiments were carried out on VoltaLab40 PGZ301 potentiostat/ galvanostat (Radiometer Analytical SAS, France) using a three-electrode electrochemical cell of 25 mL containing a glassy carbon (GC)-working electrode with a geometric area of 0.013 cm2, a platinum wire as counter (auxiliary) and Hg/Hg2Cl2 paste-covered wire as reference electrode. The voltammogram of a given amount of the test solution was recorded in the absence of DNA, after degassing the solution from oxygen via bubbling nitrogen gas for at least 15 min. The manipulation was then repeated for solutions with 100 μM of the studied compounds and increasing concentration of DNA. The working electrode was polished after every electrochemical assay. Absorption spectra were performed on a UV–Vis spectrometer (Shimadzu 1800, Japan).

The electronic spectrum of 1 mM of New-FD was first recorded at 298 K. The spectroscopic response of amount of New-FD was then measured after the addition of gradually increasing concentration of DNA solution. Each sample was permitted to equilibrate for at least 5 min before every spectroscopic measurement.

3.Obtained results from three techniques

3.1. Cyclic voltammetric studies

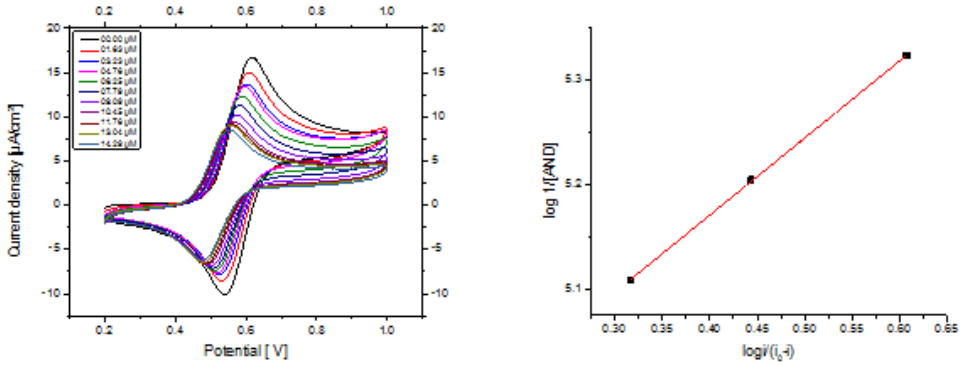

Fig.2. Cyclic voltammograms of 100 µM of New-DF recorded at 0.1 V s−1 potential sweep rate on GC disk electrode at 298 K in the absence and presence of increasing concentration of DNA with supporting electrolyte 0.1 M TBATFB. Inset: Plots of 1/1 − (i/i_0) versus 1/[DNA] used to calculate the binding constants of New-DF with DNA.

3.1.1. Binding constant and free energy

Table 1. Binding constant and binding free energy value for New-FD ligand with DNA from CV data at T = 298 K.

Adduct	Equation	R^2	K(M-1)	-ΔG (KJ mol−1)
New-DF-DNA	y = -10.52x – 0.66	0.99	5.92×10^4	26.40

3.1.2. Binding site size

Table 2. Binding site size value of compound New-FD obtained using the Plot of Cb/Cf versus [DNA].

Adduct	Equation	R^2	s
New-DF-DNA	y = 0.08x -0.13	0.98	0.17

3.1.3. Diffusion coefficients

Table 3. Diffusion constants values of the free and DNA-bound forms of New-FD.

Adduct	Equation	R^2	D(cm^2/s)
New-DF	y = 1.09x +6.30	0.98	2.18×10^{-10}
New-DF-DNA	y = 1.12x +1.61	0.98	1.10×10^{-10}

3.2. UV–visible spectroscopic study

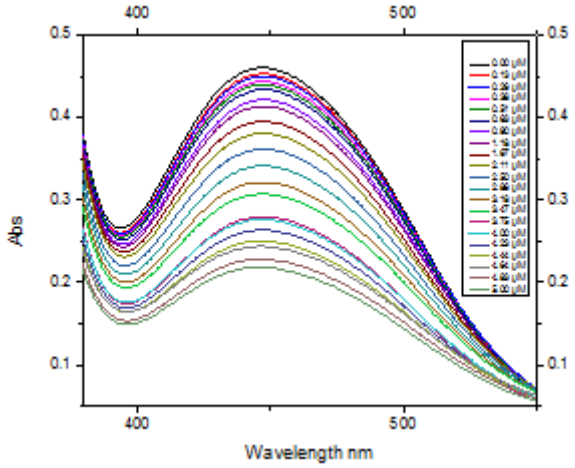

Fig.3. UV–Vis absorption spectra of 1 mM of New-FD in the absence and presence of DNA, at 298 K. Inset: Plots of A0/(A − A_0) versus 1/[DNA] used to calculate the binding constants of ligand New-FD with DNA..

Table 4. Binding constant and binding free energy value for New-FD compound with DNA from UV–visible spectrophotometric data at 298 K.

Adduct	Equation	R^2	K(M-1)	-ΔG (KJ mol–1)
New-FD-DNA	y = -10.52x – 0.66	0.99	6.93×10^4	25.98

3.3. Molecular docking study

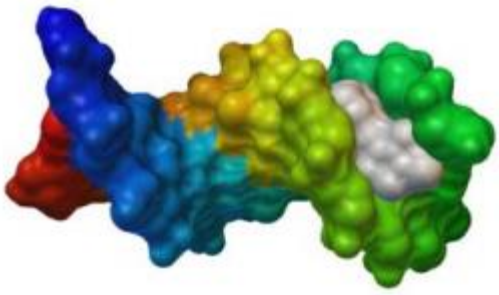

Figure .4. Surface view of docked New-DF with DNA.

Table 5. Binding energy value obtained for New-FD-DNA adduct by molecular docking approach**.**

Adduct	$K(M^{-1})$	$-\Delta G$ (KJ mol^{-1})
New-FD-DNA	*6*.14x10^4	−26.71

4. Conclusion

Voltammetric and spectroscopic assays accompanied by molecular docking calculations were used to study the interaction of potential anticancer agent new-phenyl ferrocene with DNA.

The experimental results and molecular docking study indicate that a ligand possess significant binding affinity with DNA via electrostatic interactions as the dominant mode Furthermore the order of magnitude of binding energy and the small value of binding site size obtained from voltammetric measurements confirm the electrostatic interaction

new-phenyl ferrocene with DNA. These findings clearly indicate that a studied ligand can cause conformational changes in the structure of DNA, subsequently slowing down the cell replication process and eventually preventing the cell death.

References

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