Research Article

Chemical Review and Letters
journal homepage: www.chemrevlett.com
ISSN (online): 2645-4947 (print) 2676-7279

Thermodynamic and reactivity descriptors Studies on the interaction of Flutamide anticancer drug with nucleobases: A computational view

Maedeh Kamel[a, *], Kamal Mohammadifard[b]

[a]*Department of Chemistry, Payame Noor University, PB BOX 19395-4697 Tehran, Iran*

[b]*Department of chemical engineering, Ferdowsi University of Mashhad, Mashhad, Iran*

ARTICLE INFO

Article history:
Received 23 November 2020
Received in revised form 25 December 2020
Accepted 30 December 2020
Available online 01 January 2021

Keywords:
Density functional theory
Flutamide drug
HOMO-LUMO
Chemical Reactivity

ABSTRACT

In this work, the interaction between Flutamide (FLU) anticancer drug with nucleobases such as cytosine, thymine, uracil and adenine was studied by density functional theory (DFT) methods from a thermodynamic point of view. The Gibbs free energy (ΔG) and enthalpy (ΔH) of C-FLU, T-FLU, U-FLU and A-FLU complexes were computed and demonstrate that the stronger interaction between cytosine and FLU and the adsorption of the drug on the bases proceeds spontaneously. The negative value of ΔH indicates that the adsorption of FLU drug on the cytosine, thymine and uracil bases are exothermic, these results confirmed ΔE results. During the interaction of Flutamide drug with nucleobases, the energy levels of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) were significantly changed. The values of the energy gap (E_g) reduced during the adsorption of the FLU drug onto bases which confirmed that the reactivity of the resulted complex increase upon adsorption. On the other hand, as a result of theoretical calculations, the values of the Eg for the Base-FLU structures in water solution are decreased in comparison to the corresponding values in the gas phase, indicating more the reactivity of the studied complexes in the aqueous medium.

1. Introduction

Study on the interaction between drugs and DNA [1-3] represents a great interest in many aspects of today biochemical research not only in understanding the mechanism of action of the drug, but also for the design of new drugs [4]. However, mechanism of interactions between drug molecules and DNA is still relatively little known. It is necessary to introduce more simple methods for investigating the mechanism of DNA-drug interaction. The understanding of the mechanism of interaction will promote designing of new DNA-targeted drugs.

In recent years there is a growing interest in the investigation of interaction between anticancer drugs and DNA targeted molecules. This research is currently under intense investigation owing to their therapeutic value as anti-cancer agents [5,6]. Cancer, in which cells grow and divide abnormally, is one of the primary diseases with regards to how it responds to drug delivery [7].

Flutamide (4-nitro-3-trifluoromethylisobutylanilide) a synthetic antiandrogenic compound with therapeutic use in prostatic cancer has been electrochemically studied to propose a new electroanalytical alternative for its quantitative determination in pharmaceutical forms [8]. Flutamide is used as antineoplastic and antiandrogen drug. It is a powerful nonsteroidal androgen antagonist [9] which is used to treat prostate cancer and is believed to block androgen receptor sites. Vargas et al. [10] have investigated photochemistry and phototoxicity studies of Flutamide, a phototoxic anti-cancer drug. Payen et al. [11] studied synthesis and biological activity of ferrocenyl derivatives of the non-steroidal antiandrogens Flutamide and bicalutamide.

* Corresponding author. Tel.: +989113239517; e-mail: kamel.chemist@gmail.com