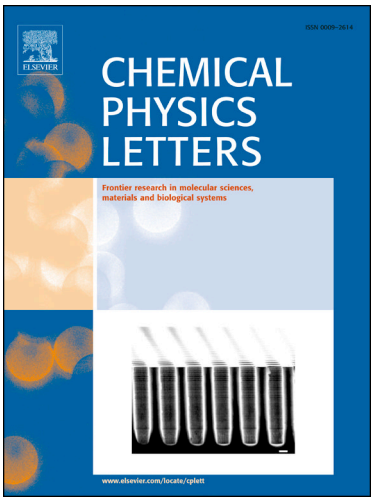

Research paper

A theoretical investigation on bio-transformation of third generation anti-cancer drug Heptaplatin and its interaction with DNA purine bases

Venkata P. Reddy B., Subhajit Mukherjee, Ishani Mitra, Sankar Ch. Moi

PII: S0009-2614(17)30985-5
DOI: https://doi.org/10.1016/j.cplett.2017.10.050
Reference: CPLETT 35199

To appear in: *Chemical Physics Letters*

Received Date: 23 August 2017
Accepted Date: 24 October 2017

Please cite this article as: V.P. Reddy B., S. Mukherjee, I. Mitra, S.C. Moi, A theoretical investigation on bio-transformation of third generation anti-cancer drug Heptaplatin and its interaction with DNA purine bases, *Chemical Physics Letters* (2017), doi: https://doi.org/10.1016/j.cplett.2017.10.050

A theoretical investigation on bio-transformation of third generation anti-cancer drug Heptaplatin and its interaction with DNA purine bases

Venkata P. Reddy B., Subhajit Mukherjee, Ishani Mitra and Sankar Ch. Moi*

Department of Chemistry, National Institute of Technology Durgapur, Durgapur-713209, West Bengal, India.

*Corresponding author, E-mail address: sankarmoi67@yahoo.com

Keywords: Anti-cancer drug, Heptaplatin, Hydrolysis mechanism, Biotransformation, Guanine/Adenine, Density functional theory.

A B S T R A C T

Heptaplatin is an approved platinum based cytostatic drug for the treatment of gastric cancers. The hydrolytic bio-transformation of Heptaplatin and the platination processes of guanine(G) and adenine(A) with resulting mono and di-aquated species of Heptaplatin have been investigated using density functional theory (DFT) combined with the conductor like dielectric continuum model (CPCM) approach, to spotlight the drug activation energy profiles and their binding mechanisms. The stationary points on the potential energy surfaces were fully optimized and characterized. The mono-functional binding of Heptaplatin, guanine as target over adenine due to electronic factors and more favorable hydrogen-bonds pattern.

1. Introduction

Platinum chemistry is one of the widespread and versatile fields of chemistry, because of Pt reactivity with many organic and inorganic molecules to give a enriched the field of bio-inorganic domain[1]. Cisplatin and next generation platinum based anticancer drugs are mostly used in chemotheraphatic agents.[2] It is generally accepted that these platinum complexes undergo hydrolysis before reaching to its cellular target DNA. Thus, more interest has been focussed on kinetics of bio-tranformation of these complexes in various solution conditions [3-5] has become a weighty part of contemporary medicinal inorganic chemistry. [6,7]

Heptaplatin is a third generation anticancer drug, was developed by Sunkyong industry research centre in Korea under the name SKI 2053R and entered clinical trials in the 1990s