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A DFT approach on tioguanine: Exploring tio-tiol tautomers, frontier molecular orbitals, IR and UV spectra, and quadrupole coupling constants

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ABSTRACT

Tioguanine (TG) is a drug for medication of several types of cancers with favorable efficacy and unfavorable side effects. TG is a modification of guanine nucleobase including two fused heterocyclic rings easy for contributing to tautomerism mechanism, which was investigated in this work based on density functional theory (DFT) calculations. The tautomerism processes of tio-tiol conversion could show serious impacts on the expected function of TG, in which the results of this work indicated that such tautomers could be easily formed with small magnitude of switching energy between the tautomers. Frontier molecular orbitals analyses showed serious variations in the electronic features of TG molecules in tautomeric forms, in which the results were further described by the atomic scale quadrupole coupling constant (Q_{cc}) evaluations. Although the switching energy was small enough to see all the tautomers in the same mode, but molecular and atomic scale features revealed different achievements for such systems as possible reasons of side effects arising during medications. As a final remark of this work, it could be mentioned that TG drug might be modified to show improved efficacies for the patients with lower side effect impacts; otherwise, the tautomeric processes could lead to existence of different side effects.

1. Introduction

Pioneering work of nucleic acid recognition by Watson and Crick in 1953 raised a huge number of attempts by other researcher to investigate various aspects of these substances of building blocks of life [1]. Exploring structural stabilities, interacting possibilities, synthetic derivatives, and pharmaceutical relatives have been all considered by researchers of multidisciplinary fields after such pioneering work [2–5]. Adenine, guanine, cytosine, thymine and uracil are main five nucleobases of nucleic acids, in which their synthetic relatives have been arisen for biomedical applications in living systems [6–10]. Especially in those diseases related to genes functions such as cancer, the synthetic nucleobases drugs have been seen very much useful for therapeutic medications [11]. Fluorouracil (5-FU) is a remarkable example of such nucleobases drugs, which has been used for therapy of cancer for years [12]. Another example is tioguanine (TG), also known as 6-thiogunaine or thioguanine, which is a synthetic derivative of guanine by replacing sulfur atom instead of oxygen atom of purine nucleobase [13]. TG has been used for years in treatment of several types of cancers especially those of leukemia family [14]. TG has been categorized for safe mode medication of cancer patients to save their life; however, serious side effects have been seen for long-term use or in the period of pregnancy [15]. Knowing details of structural features could somehow help to learn about different possible functions of a substance, in which the head topic is defined as structure–activity relationship (SAR) [16]. To this aim, earlier works have examined different sides of TG to provide useful results for this favorable substance of cancer medication but the examination has been still under progress [17–20]. One of the important structural features of such nucleobase organic compounds is their participation in tautomerism processes, in which change of structural and electronic properties in comparison with the original structure could yield unwanted activities for new tautomers even toxic impacts [21]. Movement of one hydrogen atom among the atomic sites of heterocyclic ring could yield several other structures with serious deviations of properties in comparison with each other, in which

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