Study of the Biological Interaction of Some Fullerene-based Systems

THESIS

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TITLE OF THE THESIS

"Study of the Biological Interaction of Some Fullerene-based Systems"

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بسم الله

الرحمن

الرحيم

وبه نستعين

To

My Father& Mother

and

My Brothers& Sisters

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رسالة مقدمة

إلى

كلية العلوم- جامعة القاهرة

لنيل درجة الماجيستير فى العلوم

من

نهى على محمد صالح

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الملخص العربى

Abstract

In the last decade there has been increasing interest in the fullerene-based systems. This is because of its efficient role in a variety of applications such as superconductors, sensors, catalysts, optical and electronic devices. Also it has biological activities such as antioxidants, antiapoptosis, neuroprotective, DNA photocleavage, and antimicrobial activities. It is also used as enzyme inhibitor and Magnetic Resonance Imaging (MRI) contrast agent.

The present work is a trial to benefit from the properties of fullerene-based systems, C_{60}, in the treatment of AIDS; one of the most widely spread diseases that has shown resistance towards many drugs and is still considered a challenge for scientists and doctors. The approach of this work involves the use of a number of fullerene-based derivatives which are expected to have potential biological activity to be used as proposed Human immunodeficiency virus protease (HIV-PR) inhibitors.

This is carried out using an Ab-Initio molecular modeling method of some fullerene-based derivatives and its interaction with aspartic acid; the main amino acid in the active site of HIV protease.

Molecular modeling served in performing energy minimization for each of the fullerene-based derivatives, aspartic acid, and their interaction. It also provides the corresponding vibrational spectra and Quantitative structure-activity relationship (QSAR) properties.

Computational results show that the [C_{60}] fulleropyrrolidine-1-Hydroxy-acetic acid 2-(2-hydroxy-acetoxy)-phenyl ester [C_{60}–C_2H_4N–(4-$OCOCH_2OH$) C_6H_4] has the most favorable HIV inhibition parameters among the investigated compounds. These parameters include maximum stability of the interaction with aspartic acid, lowest optimization energy, high dipole moment and maximum solubility. Accordingly, a promising anti HIV-Protease structure is developed and presented in this work.

1. Introduction and literature review

1.1. Fullerene Based Systems:

1.1.1. Discovery and synthesis of Fullerene-based systems.

Fullerene-based systems are the third allotropic form of carbon (unlike graphite or diamond) which was discovered in 1985 by Kroto, Smalley and their collaborators in molecular beam experiments. This discovery led to the award of Noble Prize in Chemistry to Curl, Kroto and Smalley in 1996. Stable cluster consisting of 60 carbon atoms was produced during their experiments aimed at understanding the mechanisms by which long-chain carbon molecules were formed in interstellar space and circumstellar shells ***(Kroto et al 1985)***. The technique which Kroto et al used to produce C_{60} involved the vaporization of carbon species from the surface of a sold disk of graphite into a high-density helium flow, using a focused pulsed laser. The vaporization laser was the second harmonic of Q-switched Nd:YAG producing pulse energies of ~30 mJ. The resulting carbon clusters were expanded in a supersonic molecular beam, photoionized using an excimer laser, and detected by time-of-flight mass spectrometry. The vaporization chamber is shown in figure **1.1.**

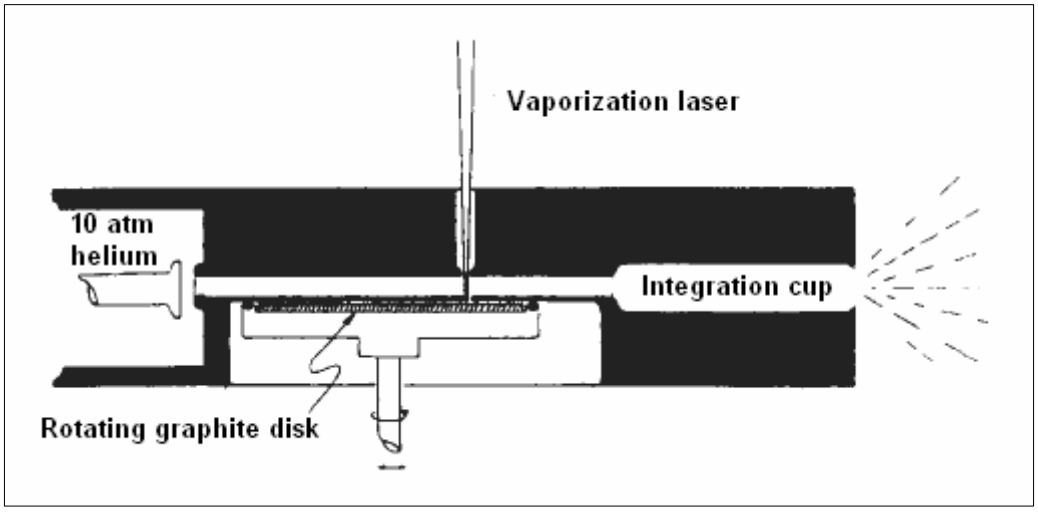

Figure 1.1. Schematic diagram of the pulsed supersonic nozzle used to generate carbon cluster beam *(Kroto et al 1985)*.

In 1990, Krätschmer and Huffman discovered a simple method to isolate and produce macroscopic quantities of fullerene-based system (C_{60}).The starting material was pure graphitic carbon soot with a few percent by weight of fullerene -based system C_{60} molecules. It was produced by evaporating graphite electrodes in an inert atmosphere of~100 torr of helium. The resulting black soot was gently scraped from the collecting surfaces inside the evaporation chamber and dispersed in benzene. The material giving rise to the spectral features attributed to C_{60}, dissolved to produce a wine-red to brown liquid, depending on the concentration. The liquid was then separated from the soot and dried using gentle heat, leaving a residue of dark brown to black crystalline material. This material had been analyzed by mass spectroscopy at several facilities, x-ray diffraction, infrared spectroscopy and electron diffraction. These analyses indicated that this material contain large amount and pure fullerene-based system C_{60} ***(Krätschmer et al 1990)***.