Recommendation

Investigation on the interaction of dietary phenolic acids and their derivatives with biologically significant molecules: A multi spectroscopic analysis

Thesis submitted for the partial fulfillment of the requirements for the degree

Doctor of Philosophy in Science

by

Prasenjit Mondal

Under the Supervision of

Dr. Adity Bose

Department of Chemistry

Faculty of Natural and Mathematical Sciences

Presidency University

Kolkata, India

2023

Summary and conclusion

The chemical species that act as free radicals are formed during our daily metabolic processes. These free radicals affect the tissues and biological macromolecules and, finally, cause various health disorders like diabetes, cancer, neurodegenerative diseases, etc. The protection of biological macromolecules like DNA from the damaging effects of such free radicals is crucial for the survival of a biological system. Although several synthetic drugs are now available which protect the oxidative damage but the prolonged use of them may result in a number of chronic health issues. Hence, an alternate solution to solve the issue is to consume natural supplements from food and traditional medicine, but the main disadvantage of these natural supplements is their low water solubility. The most common and well-known natural supplements that are used as traditional medicine are phenolic acids (PAs) because they are found naturally in many fruits and vegetables as well as in your daily diet.

The thesis describes the physico-chemical investigation of natural PAs with DNA as well as synthesis of PAs based metal nanoparticle and its application on our environment. The main disadvantage of PAs is their low water solubility; however, it is now possible to increase the water solubility of PAs by using milk protein to improve their bio-efficacy. The following discussion summarizes the work done during this period.

Chapter 1 includes a general introduction as well as the scope and goal of the thesis. This chapter also contains a brief survey of the literature to assist readers in understanding the work's background.

Chapter 2 gives a brief account of the theories of various analytical techniques as well as the characterization of different interactions and physical states. This chapter also focused on the chemical name and their respective molecular formula.

In Chapter 3A, different methods have been used to investigate the interaction of sinapic acid (SA), a hydroxycinnamic acid, with the DNA of the calf thymus (ct-DNA). Basically, it has been found that SA interacts with DNA through a minor groove. The ground state interaction occurs between SA and ct-DNA with the spontaneous binding process. The involvement of hydrogen bonding and weak van der Waals forces play an important role here. All these experimental findings are supported by the theoretical study. Finally, the gel electrophoresis result clearly indicated that SA can protect DNA damage from UVB radiation.

In Chapter 3B, we have applied different solvent system for SA delivery and its effective dose against the radiation-induced (UVB) cellular damage in vitro system. Antioxidant activity of SA in different solvent media has been shown.

Chapter 4 describes the preparation and characterization of SA based Ni nanoparticle and detection of MnO_4^- ions selectively. The detection of MnO_4^- ions is accomplished using UV-Vis spectroscopy. The prepared nanoparticles (NPs) can sense MnO_4^- ions at micromolar range (μM). The sensing mechanism was established through various analytical tools.

In Chapter 5, I have dissolve SA in beta-casein and subsequent work have been done. This β-CN entraps the SA and increases its water solubility as well as increases the bio-efficacy of the SA. The intrinsic fluorescence of β-CN was quenched by SA through static quenching mechanism. The antioxidant activity of the β-CN-SA system is greater than that of free SA. Surprisingly, a prolonged release of SA from the β-CN micellar cavity was observed in the simulated gastric and intestinal fluid, which attributed to the improved bio-efficacy of SA.

In Chapter 6, we looked into the interaction between gallic acid (GA), a hydroxybenzoic acid, and ct-DNA. The experimental results based on spectroscopic and theoretical tools suggested the occurrence of minor groove binding interactions. The interaction is spontaneous, and the involvement of H-bonding as well as van der Waal's force was evident from theoretical studies.

The overall work proves that the PAs interact biological macromolecules like ct-DNA. We also hope that our research will lead to the development of a next-generation therapeutic drug, the design of a new efficient drug molecule, and the development of methodology for studying the drug's interaction with DNA.

Limitations and future scopes

Limitations

This section discusses the limitations that we had to work within throughout the course of the thesis.

- One of the studied compounds, gallic acid (GA) absorbs in the similar range of wavelength with that of DNA, which restricted us to observe GA-DNA interaction in the ground-state.
- The fluorescence emission of GA and BSA falls in the same region, which restricted us to observe the interaction between GA and BSA.
- Interaction mechanism of dietary PAs with Ct-DNA could have been enhanced further with the assistance of certain advanced instruments/methods.
- Sinapic acid (SA) is weakly fluorescent and has a very short excited-state lifetime, which hampered the lifetime measurements of SA-DNA system.

Future scopes

Some future aspects of these works are as follows

- Synthesis of PEGylated-SA can be performed to increase the water solubility of SA, which can lead to its enhanced bio-efficacy.
- Further modification of the β-CN system can be done in order to achieve better results with targeted delivery.
- Further modification of PAs can be done, e.g., metal complexation, attaching to polymer backbone, synthetic modifications, etc., in order to enhance the applicability of PAs.