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A computational investigation on the structure, global parameters and antioxidant capacity of a polyphenol, Gallic acid

Vijisha K. Rajan, K. Muraleedharan *

Department of Chemistry, University of Calicut, Malappuram 673635, India

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ABSTRACT

A computational DFT-B3LYP structural analysis of a poly phenol, Gallic acid (GA) has been performed by using 6-311++ G (df, p) basis set. The GA is a relatively stable molecule with considerable radical scavenging capacity. It is a well known antioxidant. The NBO analysis shows that the aromatic system is delocalized. The results reveal that the most stable radical is formed at O_3-atom upon scavenging the free radicals. Global descriptive parameters show that GA acts as an acceptor center in charge transfer complex formation which is supported by ESP and contour diagrams and also by Q^{max} value. The GA is a good antioxidant and it can be better understood by HAT and TMC mechanisms as it has low BDE, $\Delta H_{acidity}$ and $\Delta G_{acidity}$ values. The ΔBDE and ΔAIP values also confirm that the antioxidant capacity of GA can be explained through HAT rather than the SET-PT mechanism.

1. Introduction

Gallic acid (3,4,5-trihydroxybenzoic acid) (GA) and its derivatives are found in gallnuts, oak bark, sumac, grapes and tea leaves as one of the main phenolic components (Chanwitheesuk, Teerawutgulrag, Kilburn, & Rakariyatham, 2007). Biological studies show that GA has various properties, including anti-fungal, anti-viral, antioxidant and anti-cancer activities. GA is also employed as a source material for inks and paints, and as an antioxidant in food, in cosmetics and in the pharmaceutical industry (Tekale & Pangrikar, 2011). In the medicinal view, antioxidants in general are used to prevent the oxidative damage that takes place in biomolecules by scavenging the reactive oxygen species (Embuscado, 2015; Sadasivam & Kumaresan, 2011).

Oxygen being the ultimate electron acceptor in electron flow systems to produce energy in the form of ATP, the oxidation reactions is indispensible part of aerobic life. But the electron flow system when uncoupled, generates free radicals mostly oxygenated species called Reactive Oxygen Species (ROS) and these highly reactive species, including superoxide radicals, peroxy radicals, alkoxy radicals, etc, causes damages to life activities. Apart from the positive roles of ROS like involvement in energy production, phagocytosis, regulation of cell growth and intracellular signalling, they are very damaging and play negative roles like attacking lipids in cell membranes, proteins in tissues or enzymes, carbohydrates and DNA to induce oxidations, which cause membrane damage, protein modification and DNA damage. This oxidative damage has an essential role in aging and several degenerative diseases associated with it, such as heart disease, cataracts, cognitive dysfunction and cancer (Pietta, 2000). The neurodegenerative diseases are also related to the free radical reactions. For example in Parkinson disease the oxidation of dopamine releases the ROS and their unbalanced over production causes oxidative stress which ultimately leading to the neuronal death (Lu, Nie, Belton, Tang, & Zhao, 2006). Antioxidants are compounds which protect the cell from the damage caused by chemical reactions involving free radicals. In this scenario it is very important to include fruits and vegetables containing antioxidants in the diet. They either stabilize the free radicals or deactivate them before they attack cells. Antioxidants are the first line of defense against the ROS and are critical for maintaining optimal cellular and life activities.

Abbreviations: GA, Gallic acid; DFT, density functional theory; NBO, Natural Bond Orbital; ESP, electrostatic potential; SDF, standard data file; GJF, Gaussian Job File; HOMO, Highest Occupied Molecular Orbital; LUMO, Lowest Unoccupied Molecular Orbital; AIP, Adiabatic Ionization Potential; ETE, Electron Transfer Enthalpy; BDE, bond dissociation energy; HAT, hydrogen atom transfer; SET, single electron transfer; SET-PT, single-electron transfer followed by proton transfer; PDE, proton dissociation energy; SPLET, sequential proton loss electron transfer; PA, proton affinity; TMC, Transition Metals Chelation; VIP, vertical ionization potential; VEA, vertical electron affinity; ROS, reactive oxygen species.

* Corresponding author.
E-mail address: kmuralika@gmail.com (K. Muraleedharan).

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In order to protect the body from the oxidative stress caused by ROS, humans evolved a well sophisticated and complex antioxidant protective system. It involves a variety of components, both endogenous and exogenous in origin, that function interactively and synergistically to neutralize free radicals. They include nutrient-derived antioxidants like vitamin C & E, antioxidant enzymes (glutathione, superoxide dismutase, peroxidases), metal binding proteins (ferritin, lactoferrin, albumin & ceruloplasmin) etc, (Percival, 1998).

GA and their derivative are widely present in the plant kingdom and represent a large family of plant secondary metabolites and hence natural antioxidants (Lu et al., 2006). Poly-phenols or phenolic compounds are capable of exhibiting a lot of bioactivities like antioxidant property (Rice-Evans, Miller, & Paganga, 1997). These are due to their radical scavenging capacity which is based on the availability of —OH groups and on the possibility of stabilization of the resulting phenolic radicals through hydrogen bonding or extended electron delocalization (Bors, Heller, Michel, & Saran, 1990). So the study of electronic and molecular properties is of great importance that helps for the better understanding of the mechanism of bioactivity. Many experimental and theoretical works has been reported in this area (Jiménez-Zamora, Delgado-Andrade, & Rufián-Henares, 2016; Racicot et al., 2012). The Experimental methods only give the BDE value of the weakest —OH bond in the molecule whereas the theoretical methods give BDE values of all the —OH bonds present in the molecule. This enables the comparison study of the radical scavenging activity of the molecule at different sites. This advantage of theoretical methods over the experimental methods drives the chemists to carry out theoretical/computational methods for studying the antioxidant properties of bioactive molecules.

The present work employed computational methodologies for the structural studies. Computational Chemistry is the study of problems based on quantum mechanical calculations. It simulates the chemical structures and reactions numerically based on fundamental laws of physics. It opens new frontiers for the chemist to study chemical phenomena by running calculations on computers rather than by examining reactions and compounds experimentally. Computational methods are green less time consuming and easy to process. The recent impact of DFT methods, similar to ab-initio method in many ways, by the development of Quantum chemical calculation is very considerable (Clementi & André, 2012). DFT is an important computational technique for calculating geometries and energies of molecules. Unlike the other computational techniques, DFT is not based on wave function, but rather on electron density probability function or simply the electron density function (Lewars, 2004; Young, 2001). Before going to the details of antioxidant studies of molecules, it is better to get a detailed awareness about the structure of molecule under study. Density Functional Theory (DFT) is a widely used computational tool because of its high degree of predicting power and accuracy. In order to understand the structure of a molecule, a number of factors must be known. These include the geometrical parameters, global descriptive parameters, bond order, hybridizations, molecular orbital energies, etc. The present work has employed the structural analysis of the poly phenol, GA. The geometrical parameters and global properties are studied by DFT-B3LYP level of theory. The bond orders, hybridizations and occupancies of different bonds in the molecule are computed through Natural Bond Orbital (NBO) analysis. The frontier molecular orbitals are analyzed and the charge distribution in the GA molecule is studied through ESP and contour diagrams. The nature of reactivity, whether Gallic acid donate or accept electrons is predicted through this work. From the NBO analysis bond strength of molecule has been analyzed and the stable radical is predicted. There are five mechanisms available for explaining the antioxidant capacity (Leopoldini, Russo, & Toscano, 2011b). The present work employed these mechanisms and the most preferred mechanism is selected to explain the antioxidant capacity of GA.

2. Materials and methodology

2.1. Materials

The present work has used a computational approach to the structural analysis of GA. The input structures are drawn by using the Gaussview-5.0 graphical user interface. All the computational works have been carried out through Gaussian 09 software package (Frisch et al., 2004). Some of the structures are taken from the pubchem database (Bolton, Wang, Thiessen, & Bryant, 2008) and these are in SDF file format. To convert these SDF files to GJF (Gaussian Job File) input files an application called OpenBabel (O'Boyle et al., 2011) has employed.

2.2. Computational methodology

The present study employed a DFT based structural analysis of a poly phenol Gallic Acid (GA). The level of theory adopted is B3LYP, which consists of Becke's exchange functional (Becke, 1993) in conjunction with Lee-Yang–Parr correlational functional (Lee, Yang, & Parr, 1988) and the basis set used is 6-311++G (df, p). All the computational works are carried out through Gaussian 09 software package.

At first a potential energy scan is performed on the structure of GA to obtain the stable conformer. Then the lowest energy conformer is used for the further studies. The structure of GA is optimized using 6-311++G (df, p) basis set and geometrical parameters (at 298 K) are evaluated. The following structural analysis have been employed in the present work.

2.2.1. Frontier molecular orbital analysis

Frontier molecular orbitals (HOMO and LUMO) of the optimized GA are analyzed and band gap is calculated. Electrostatic potential maps, also known as electrostatic potential energy maps, or molecular electrical potential surfaces, are analyzed which illustrate the charge distributions of a molecule three dimensionally. These maps allow us to visualize variably charged regions of a molecule. Knowledge of the charge distributions can be used to determine how molecules interact with each other. They enable us to visualize the charge distributions of molecules and charge related properties of molecules. In organic chemistry, electrostatic potential maps are invaluable in predicting the behavior of complex molecules. Electrostatic potential energy is fundamentally a measure of the strength of the nearby charges, nuclei and electrons, at a particular position.

2.2.2. Global descriptive parameters

The utility of global descriptive parameters of a molecule gives an idea about the relation between the chemical reactivity of the molecule and its sensitiveness to structural perturbations and responses to the changes in external conditions. The global descriptive parameters include the chemical potential, electronegativity, hardness, softness, electrophilicity index, etc. These quantities correspond to the linear responses of the electron density with respect to the changes in the external potential and number of electrons (Srivastava, Srivastava, & Alam, 2014). Thus global descriptors are of particular relevance in comparing the properties of different molecules. The global hardness reflects the overall stability of the system (Kar, Chandrakumar, & Pal, 2007). The chemical hardness fundamentally signifies the reluctance towards the deformation or polarisation of the electron cloud of the atoms, ions