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The natural food colorant Peonidin from cranberries as a potential radical scavenger – A DFT based mechanistic analysis

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ABSTRACT

A theoretical evaluation of the antioxidant property of a natural food colorant Peonidin has been performed. The most suitable mechanism for explaining the radical scavenging capacity of Peonidin is the Hydrogen Atom Transfer and the most active site for radical formation is position 3 and is confirmed through Mulliken charge analysis, pKa value evaluation, Bond Dissociation Energy values, and Natural Bond Orbital analysis. Position 3 and 5 in Peonidin exists in blood as deprotonated as their pKa values are lower than the pH of blood. Peonidin is highly reactive than Quercetin and less stable than flavan-3-ols due to the small band gap. Global descriptor analysis shows that PN prefers to accept electrons than to donate. The effect of number of –OH groups and the nature of substituents are well explained through this work.

1. Introduction

About 33 years ago; i.e., in 1985, the concept of Oxidative Stress (OS) has been introduced in the Redox biology and medicine as the introductory chapter 1 in the book 'Oxidative Stress' (Sies, 1985). Later in a review article on 'Biochemistry of oxidative stress' (Sies, 1986), explain the world of antioxidant and their influence in biological system and then onwards 'Redox biology' becomes an interesting area of research among various disciplines like Chemistry, Medicinal Chemistry, Pharmaceutics, Biology, Radiation biology, etc.

The OS is the dangerous situation resulting from the generation of free radicals in the biological system. These free radicals may be Reactive Oxygen Species (ROS) or Reactive Nitrogen Species (RNS). The free radicals are short living fast reactive species. They react rapidly with cellular membrane and causes disorder which ultimately leads to death. In our body, the brain is the part of high metabolic rate, lipid peroxidation, etc., so that brain is highly vulnerable to OS. This drives a scientist to develop some antiradicals to treat brain injury (Masone & Chanforan, 2015). Similarly, most of the electron transport reactions are takes place in mitochondria so that most of the ROS/RNS are generated in mitochondria. Thus antiradicals targeting mitochondria have to be developed. The OS may lead the regular/normal life activities to an abnormal level and lead to AIDS, aging, arthritis, asthma, cancer, cataract, diabetes, neurodegenerative disorders, Alzheimer's, Parkinson's disease, heart failure, etc. In order to fight against these ROS/RNS, our body develops a defense mechanism in which certain substance are actively fought against the free radicals called antioxidants (Gupta & Sharma, 2006).

The substances which produced in low concentrations in our body in order to delay the OS produced as a result of oxidation of proteins/lipids, carbohydrates, DNA, etc., are termed as antioxidants. Generally, they are called radical scavengers or antiradicals. They do so either by acting as an antioxidant or as an antireductant. There are 3 categories of antioxidants namely: 1st, 2nd and 3rd line defense antioxidants. The antioxidants present in our body are Vitamin E and C. But the modern lifestyle and food habits make these antioxidants insufficient to neutralize the free radicals generated in the biological system so that we have to depend on medicines (synthetic antioxidants). But this again has some problems because synthetic antioxidants have lots of toxic side effects and are expensive too. In this scenario, chemists forced to discover some natural radical scavengers. The discovery of natural antiradicals replaces the use of synthetic antiradicals because of a number of facts. Natural antiradicals are of low cost, compatibility with dietary intake and no harmful effects in the human body (Sindhi,

Abbreviations: OS, Oxidative Stress; ROS, Reactive Oxygen Species; RNS, Reactive Nitrogen Species; PG, Pelargonidin; CY, Cyanidin; DP, Delphinidin; PN, Peonidin; PT, Petunidin; MA, Malvidin; DFT, Density Functional Theory; HF, Hartree Fock; HAT, Hydrogen Atom Transfer; ET-PT, stepwise electron transfer-proton transfer; SPLET, sequential proton loss electron transfer; BDE, Bond Dissociation Energy; PES, Potential Energy Scanning; CM, continuum models; IEF-PCM, integral equation formalism polar continuum models; SCRF, Self-Consistent Reaction Field; SE, Semi-Empirical; FMO, Frontier Molecular Orbital; HOMO, highest molecular orbital; LUMO, lowest unoccupied orbital; VIP, Vertical Ionization Potential; VEA, Vertical Electron Affinity; NBO, natural bond orbital; NAO, natural atomic orbitals; NHO, natural hybrid orbitals; SET, single electron transfer; AIP, Adiabatic Ionization Potential; SETPT, single-electron transfer followed by proton transfer; PDE, Proton Dissociation Enthalpy; PA, proton affinity; ETE, Electron Transfer Enthalpy; NPA, Natural Population Analysis

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Table 4
Bond order parameters of PN.

Bond	Bond order
O_2- H_{29}	**0.6924**
O_3-H_{30}	0.6981
O_5-H_{31}	0.7050
O_6-H_{32}	0.6991

are present in all other anthocyanidin except MV, PG, and PN where 4 —OH groups are present. In all of them, the number of —OH groups in ring B is different while that in ring A & C are same. The electron releasing groups further decreases the BDE value while electron withdrawing groups increases it. In MV two electron releasing groups (—OCH_3) are present in ring B and thus it is having low value for BDE than DP. In CY and PT the number of —OH groups are same, but the presence of one —OCH_3 group in ring B decreases the BDE value in PT. Similarly in PN and PG the number of —OH groups are same, but PN has lower BDE value. This is due to the presence of one —OCH_3 group in PN. So we can conclude that the number of —OH groups in ring B and the number and nature of substituents together determine the trend in BDE values of anthocyanidins.

3.5. Natural bond orbital analysis

The NBO analysis gives the bond order values of all the bonds in PN. As the most suitable mechanism for explaining the antioxidant property of PN is found to be HAT, studies about radicals are important. The atomic charge analysis shows that the most active site is oxygen at position 3 and also the BDE and pKa value analysis shows that this position has the lowest BDE and pKa value so that this is the site for the stable radical formation. This is confirmed by structural optimizations of radicals also. Again the strength of a bond can be found by bond order analysis also. This is carried out by NBO tool in G09 and is given in Table 4.

The Table contains bond orders of the —OH groups only. The lowest bond order has been seen on O2 i.e., at position 3. This is in agreement with the energy values obtained in the optimization studies of radicals and BDE values. So, the most active site is the —OH group at the C3 position and the radical is formed first at this position. This is in agreement with atomic charge analysis also.

4. Conclusion

A DFT based antioxidant property evaluation of a natural food colorant PN has been summarized. Like other anthocyanidins, PN also has the most active site at position 3. The most active site is confirmed through Mulliken charge analysis, pKa value evaluation, BDE values, and NBO analysis. Position 3 and 5 in PN exists in blood as deprotonated as their pKa values are lower than the pH of blood. The most suitable mechanism for explaining the antioxidant capacity of PN is the HAT mechanism and the most active site for radical formation is position 3. The antioxidant capacity of PN is compared with other anthocyanidins and the reactivity is compared with Quercetin. PN is highly reactive than Quercetin and less stable than flavan-3-ols due to the small band gap. If there is an electron transfer reaction exists, then PN prefer to accept electrons than to donate and is confirmed by global descriptor analysis. The effect of a number of —OH groups and the nature of substituents are well explained through this work. So besides the coloring capacity, PN also have radical scavenging activity. The study can be extended to metal chelation properties of PN and thereby metal catalyzed peroxidations can be prevented.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.foodchem.2018.04.074.

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