Towards Novel Anticancer Drug Design: Computational Study on the Inhibition of the Ribonucleotide Reductase by Trans-resveratrol, Trans-piceatannol and Hydroxyurea

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Ribonucleotide reductase is an enzyme that catalyzes formation of deoxyribonucleotides from ribonucleotides. I present for the first time a quantum-chemical study of the thermodynamics of reactions of naturally occurring potent inhibitors (trans-resveratrol, trans-piceatannol and hydroxyurea) of ribonucleotide reductase with tyrosine radical and cysteine radical, scavenging of whose is crucial for the inhibition of the enzyme. Density functional theory has been applied to compute the Gibbs free enthalpy changes for these reactions in the gas phase and in the presence of water medium. Various reaction pathways have been analyzed. It was found that trans-resveratrol and trans-piceatannol may be efficient inhibitors of the enzyme (trans-piceatannol more efficient than trans-resveratrol). Because inhibition of ribonucleotide reductase is essential for blockage of the cancer development pathways, the polyphenols studied may be able to block diverse processes (including cancerogenesis) by inhibition of free radical reaction steps that occur during catalytic action of this enzyme. The paper has been published in the journal 'Letters in Drug Design & Discovery'.

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