EXTENDED ABSTRACT

Journal of Medicinal and Organic Chemistry

Theoretical insights into the molecular properties of 3-(4-hydroxyphenyl)prop-2-en-1-one 4-phenyl schiff base and some of its derivatives- molecular modelling and docking studies

Oluwatoba Emmanuel Oyeneyin[1]*, Isaiah AjibadeAdejoro[2] , Samuel Babatunde Obadawo[1] , JustinahSolayide Amoko[3] , InyangOlumide Kayode[4] , Eric Oluwafisayo Akintemi[5]

[1]Theoretical and Computational Chemistry Unit, Department of Chemical Sciences, AdekunleAjasin University, Akungba-Akoko, Ondo State.
[2] Department of Chemistry, University of Ibadan, Oyo State, Nigeria
[3]Department of Chemistry, Adeyemi College of Education, Ondo, Ondo state, Nigeria.
[4]Department of Biochemistry, AdekunleAjasin University, Akungba-Akoko, Ondo State.
[5] Chemistry Unit, Department of Physical Sciences, College of Natural and Applied Sciences, Wesley University, Ondo. Nigeria

Abstract:

Structure-property relationship is important in understanding molecular behaviours and hence their probable areas of applications. 3-(4-hydroxyphenyl)prop-2-en-1-one 4-phenyl Schiff base and some of its derivatives were optimized and via the Density Functional Theory with Becke three Lee Yang Parr correlation and 6-31G* basis set. Among the molecular properties calculated were the energies of the frontier molecular orbitals (highest occupied molecular orbitals (EHOMO) and lowest unoccupied molecular orbitals (ELUMO), energy band gap (Eg), chemical hardness (η), softness (S) and hyperpolarizabilities (β). These properties provided information about the reactivities and nonlinear optical responses of the molecules. The electronic transitions were calculated with the Time-Dependent Density Functional Theory methods, the absorption maxima (λabs), vertical transition energies (ΔEge), oscillator strengths (f) and molecular orbital (MO) components with their percentage contributions were obtained. The anti-microbial efficacy of the molecules were tested against Staphylococcus aureus aminopeptidase S (AmpS) active site to predict the binding affinities. ADMEtox parameters of all the molecules were also investigated. Variations observed from the calculated molecular properties are as a result of varying substituent groups. The molecules could be used as optical limiters, they could also be used to as effective drugs against Staphylococcus aureus.

Introduction:

Heterocyclic compounds have a vital role in medicine, pharmacy and agriculture.Pyrazoles possess various important bio-medical features.This type of derivatives exhibits several therapeutic activities such as insecticidal,acaricidal, anticonvulsant, antidepressant, antiulcer, and anticancer features. So far to date, many chalcone derivatives have been synthesised and their biological activities examined. Several investigations have shown that chalcones possess important pharmacological characteristics including antitumor, anti-inflammatory, antifungal and antioxidant properties. The development of effective CA inhibitors is limited by the lack of selectivity which could lead to serious side effects. Hence, it has been of interest to us to develop not only potent hCA inhibitors but also with a promising selectivity for a specific isoform. We have previously carried out synthesis of various phenols and methoxyphenols in addition to derivatives of some natural products which possess different structures. Some of our recently synthesised compounds were found to inhibit CAs in the milimolar to low nanomolar ranges. In the current study, we focussed on the synthesis and inhibitory effects of some pyrazole derivatives against hCA I and II isoforms. Computational studies were also used to enlighten their activities based on the binding interactions with the target enzymes and their calculated molecular properties.

Azomethine or imine groups present in the organic compounds have been shown to be critical to their biological activities. In addition, the presence of nitrogen and oxygen donor atoms in such compounds makes them structurally similar to neutral biological systems and they are utilized in elucidating the mechanism of transformation of racemization reactions. Various biological activities are considered due to the presence of the azomethine linkage (>C N–) present in living systems.On the other hand, for anti-corrosion, the corrosion inhibition properties of these compounds can be assigned to its molecules with π-electrons of the imine group and π-electrons of aromatic substituents.

Schiff bases used as inhibitors may block anodic, cathodic or both sites, thus preventing the metallic substrate from undergoing hydrogen evolution reactions or metal dissolution with a predominance of film-developing surface adsorption. The corrosion inhibition efficiency of organic inhibitors has been reported to be shown by a strong affinity for inorganic surfaces, with low influences on the atmosphere. They build up protective hydrophobic film molecules adsorbed on the metallic surface, thus providing a barrier to the dissolution of the substrate in the electrolyte.

Discussion and Conclusion:

In the current study, starting from some chalcones, design, synthesis and characterisation of new pyrazole derivatives were reported. All the synthesised compounds were then evaluated for their inhibitory properties against hCA I and hCA II isoenzymes. They exhibited significant inhibitory features at low nanomolar concentrations ranging between 21.98 and 25.14 nM. Molecular docking studies further supported observed inhibitory profiles. Compound which had slight hCA I versus

hCA II selectivity, binds with hCA I in similar orientations with other compounds but it adopts different conformation in the active site of hCA II. According to the in silico molecular properties calculations, all compounds also obeyed the drug likeness properties. The new compounds presented in this study, might be promising lead compounds for the development of more selective and potent inhibitors as alternatives to the classical CA inhibitors.

.