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Full Length Research

Molecular geometry optimization of Acidifiers and Acidulants in bioactive phytochemicals present in Ethanol leaf extract of *Chromolaena odorata* and *Costus afer* sterm

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ABSTRACT: Molecular geometry optimization of Acidifiers and Acidulants in bioactive phytochemicals present in Ethanol leaf extract of *Chromolaena odorata* and *costus afer* stem was studied. The active phytochemicals, hexadecanoic acid ethyl ester, from the ethanol leaf extract of *C. odorata* and 10,12-nonacosadiynoic acid from stem of *C. afer* were studied using ArgusLab 4.0.1 software. Minimization was performed with semi-empirical Austin Model 1 (AM1) parameterization. The minimum potential energy was calculated by using geometry convergence function in ArgusLab software. Surfaces were created to visualize the highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO) and electrostatic potential mapped on electron density surface. The minimum potential energy was calculated for drug receptor interaction through the geometry convergence map. The geometry optimized energy for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid were -106.5332069610 and -157.470270 au respectively. These were the best feasible position for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid to act as acidifier and acidulant.

Key words: Acidulant, acidifier, *Chromonaela odorata, Costus afer,* geometry optimization, medicinal plant.

INTRODUCTION

Our domestic animals eat grass and plants as their source of carbohydrate, protein and fat. Compounds produced by plants have been separated into primary and secondary metabolites. The primary are molecules that are found in all plant cells and are necessary for the life of the plant such as simple sugars, amino acid, protein and nucleic acids. Secondary metabolites are restricted in their distribution, both within the plant and among the different species of plants (Evert and Eichhorn, 2013). They function as chemical signal to enable the plant respond to environmental cues, defence against pathogens. The three major classes of secondary plant metabolites are alkaloids, terpenoids and phenols (Evert and Eichhorn, 2013). There are no Veterinary Clinics in the wild but our wild animals selectively consume the plants when they are sick for self-medication (Huffman, 2003). This research is to determine the molecular geometry optimization of the secondary metabolites in *C.odorata* and *C.afer* as proposed by Gas chromatography–mass spectrometry (GCMS) analysis (Otuokere et al., 2016a,b) to find best feasible position for hexadecanoic acid ethyl ester and 10,12- nonacosadiynoic acid to act as acidifier and acidulant and use them for drug modelling for the benefit of man. GCMS analysis has been used widely by researchers for identification of phytochemicals in plants

(Igwe et al., 2016a; Igwe et al., 2016b; Ikpeazu et al, 2017b; Li et al., 2013; Purushotaman and Ravi, 2013). *C.odorata* (Siam weed) is an invasive weed of field crop in rainforest zone of Africa (CRC Weed Management, 2003). It has been reported to be the most problematic weed in Africa (Struhsaker et al., 2005). It has a fast growth rate of about 20 mm per day. It is a major pest to crops such as coconut, rubber, tobacco and sugarcane. It has a prolific seed production and its minimum life span is ten years. It grows up to 2 m tall (Struhsaker et al., 2005). The leaves of *C. odorata* are arrowhead shaped, 50 to 120 mm in length with a width of 30 to 70 mm (Struhsaker et al., 2005). *C.odorata* is a herbaceous perennial plant with an aromatic smell (Phan, 2001). Igbo's in Nigeria call it ''*Obuinenawa*'' while the Yoruba's Ijebu call it ''*Ewe Akintola*". Traditionally, *C. odorata* extract has been used in the treatment of ailments such as malaria, dysentery, toothache, diarrhea, diabetes, skin diseases, fever and wound dressing (Akinmoladun and Akinloye, 2007; Zachariades et al., 2009; Bamisaye et al., 2014). Most Nigerian populace depends on natural products in treatment of ailment because of the high cost of orthodox drugs. The healing ability of plant extract depends on their secondary metabolites. Studies have shown that *C.odorata* contains reasonable amount of flavonoids, tannis, steroids, phenolics and saponins (Bamisaye et al., 2014). In Thailand, the leaf extracts of *C.odorata* is used in the treatment of wounds, rashes, diabetes and as an insect repellent. The nematicidal, fungicidal, ethnopharmacological activity and soil fertility of *C.odorata* has been reported (Uyi et al., 2014; Lavoe, 2016). The medicinal properties of *C.odorata* extracts cannot be unnoticed in Nigeria. Its leaf extract helps in the prevention of blood loss from wounds (Iwu, 1993). Anthemintic properties of aqueous extract of *C.odorata* have also been reported (Iwu, 1993). The potentials of *C.odorata* leaf meal has been evaluated (Aro et al., 2009). From the results, the egg quality characteristics of dietary inclusion of *C.odorata* leaf meal, would not compromise egg quality characteristics like egg weight, shell thickness, albumen height and Haugh's unit (Aro et al., 2009).

C. afer on the other hand is a stout perennial rhizomatous herb that belongs to the genius *Costus* (Edeoga and Okoli, 2000). It is naturalized in Nigeria, Ghana, Niger, Guinea, South Africa and Senegal (Oliver, 1960). The Igbos in Nigeria call it "*Okpete*" or "*Okpoto*". It is called "*Kakizawaa*" by the Hausas in Nigeria, "*tete-gun*" in Yoruba language and "*Mbritem*" by Nigerian Efiks. Camerounian Anglophones call it "*Monkey sugar cane*" (Ezejiofor et al., 2013). It grows up to 4 metres tall (http://www.prota.org). The leaves are spirally arranged, tubular sheath with green-purple blotches. The spikes are conical with a length of 2.5 to 7.5 cm long (Aweke, 2007). The flowers are bisexual and the corolla tubes are 2 cm long. *C,afer* flowers and fruits vigorously throughout the year, depending on soil humidity (Aweke, 2007). In Southern Nigeria, it is regarded as a weed in rice plantation (Aweke, 2007).

Figure 1. *Chromonaela odorata* plant.

a b

Figure 2. Pictorial View of *Costus afer* (a) leaves (b) leaves and stem.

In continuation with the ongoing research on *C. odorata* and *C. afer* extract, the report on molecular geometry optimization of acidifiers and acidulants in bioactive phytochemicals as proposed by Gas Chromatography-Mass Spectrometry analysis has been included (Otuokere et al., 2016a, b). The purpose of this research is to use molecular geometry optimization, to find the geometry optimized energy for the bioactive phytochemicals present in Ethanol leaf extract of *Chromolaena odorata* and C*ostus afer* sterm which is the best feasible position for the phytochemicals to act as acidifier and acidulant.

MATERIALS AND METHOD

The pictorial view of *C. odorata* and *C.afer* is presented in Figures 1 and 2 respectively.

Geometry optimization

Geometry optimization study was performed on a window

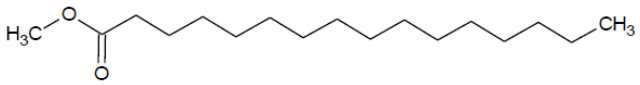

Figure 3a. Struture of Hexadecanoic acid ethyl ester.

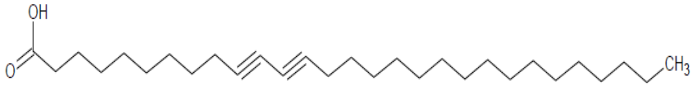

Figure 3b. Structure of 10,12- Nonacosadiynoic acid.

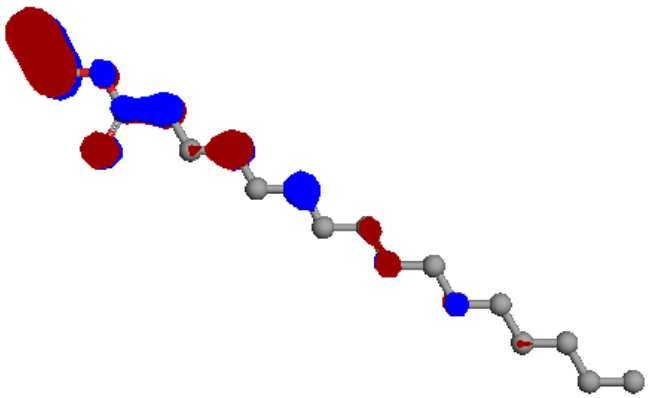

Figure 4. Highest Occupied Molecular Orbital (HOMO) of hexadecanoic acid ethyl ester.

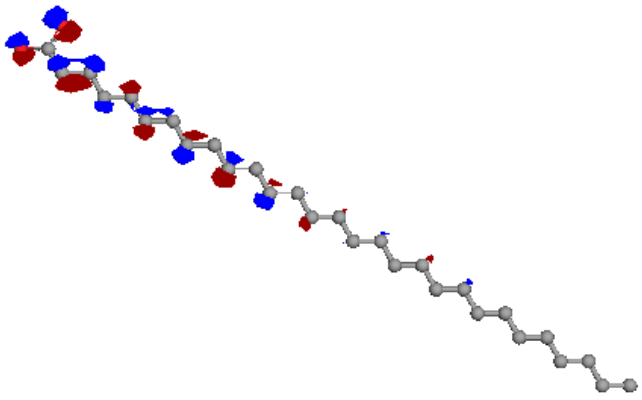

Figure 5. Highest Occupied Molecular Orbital (HOMO) of 10,12- Nonacosadiynoic acid.

based computer using ArgusLab (Thompson et al, 2007) and ACD Lab ChemSketch softwares (Advanced Chemistry Development, 2008). The chemical structures of Hexadecanoic acid ethyl ester and 10,12-Nonacosadiynoic acid (Figures 3a and b) were generated by ArgusLab, minimization was performed with semi-

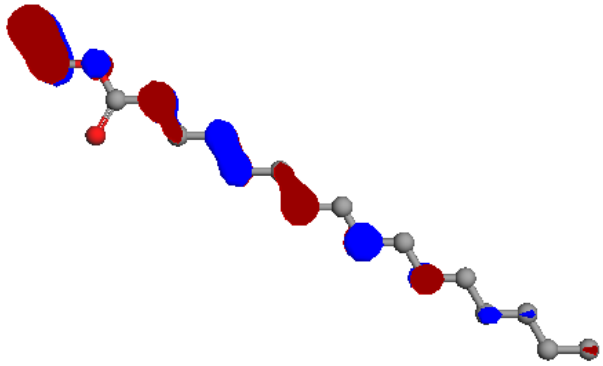

Figure 6. Lowest Unoccupied molecular orbital (LUMO) of hexadecanoic acid ethyl ester.

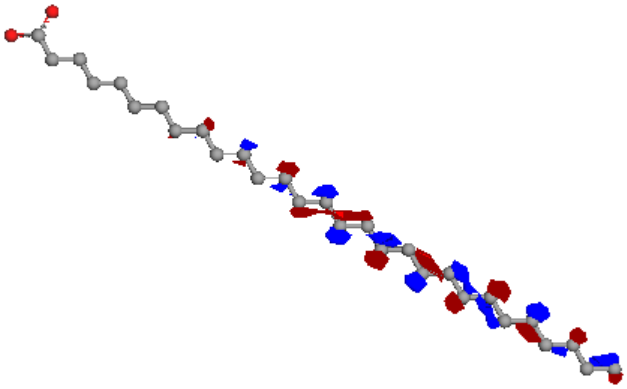

Figure 7. Lowest Unoccupied molecular orbital (LUMO) of 10,12- Nonacosadiynoic acid.

empirical Austin Model 1 (AM1) parameterization (Cramer and Truhlar, 1992) . The minimum potential energy was calculated by using geometry convergence function in ArgusLab software. Surfaces created to visualize the highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO) and electrostatic potential mapped on electron density surface. The minimum potential energy was calculated for drug receptor interaction through the geometry convergence map.

RESULTS AND DISCUSSION

The HOMO of hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid (Figures 4 and 5) is the orbital of highest energy that is still occupied, therefore energetically it is the best to get rid of electrons from this orbital. This might be merely donating negatron density to make a bond. The LUMO of hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid (Figures 6 and 7) is the lowest lying orbital that is empty, therefore energetic-

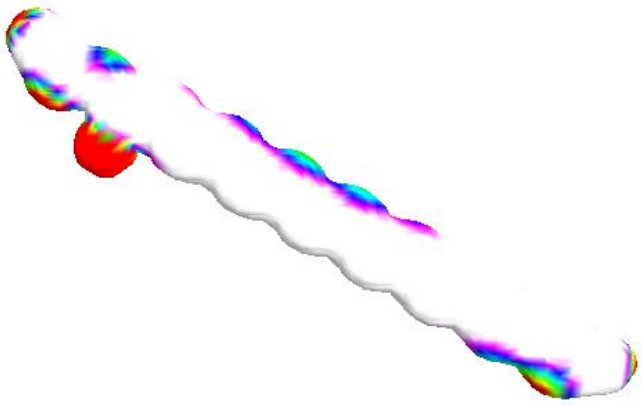

Figure 8. Electrostatic potential mapped onto electronic density of hexadecanoic acid ethyl ester.

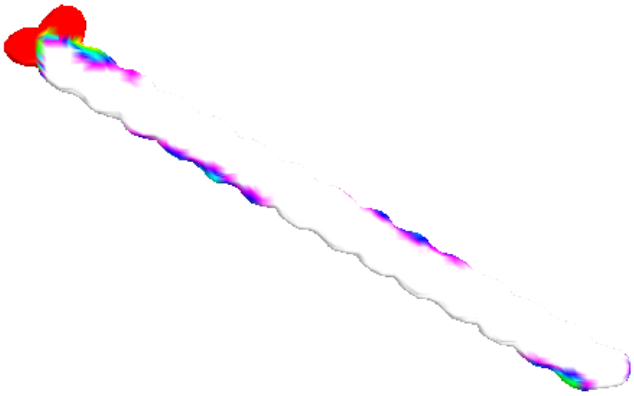

Figure 9. Electrostatic potential mapped onto electronic density of 10,12- Nonacosadiynoic acid.

cally, it is the best to feature a lot of electrons into this orbital. The Eigen values for the HOMO and LUMO of hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid, are -0.294565, -0.186697, -0.315757 and -0.187396 au respectively. ArgusLab (Thompson et al, 2007) was used in generating electrostatic potential mapped onto the electron density surface of hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid (Figures 8 and 9). Similar results were reported recently by (Ikpeazu et al., 2017a). They reported the electrostatic potential-mapped electron density surface and conformation analysis of an antidepressant, mirtazapine. In their study, electrostatic potential-mapped electron density surface showed the areas of the molecule that would be susceptible to nucleophilic and electrophilic attack.

The predicted geometry energy was -90.575172 au (-56836.830000 kcal/mol). Electrostatic potential maps are three dimensional diagrams of molecules. It permits us to check the charge distributions of molecules and charge connected properties of molecules. In chemical science, static potential maps are valuable in predicting the behavior of advanced molecules (LibreTexts, 2017). Molecular electrostatic potential maps conjointly illustrate information concerning the charge distribution of a molecule, the properties of the nucleus and nature of electrostatic energy (LibreTexts, 2017). The charged nucleus emits a radially constant field of force. The area higher than average electrostatic potential energy indicates the presence of a stronger electric charge or a weaker negative charge. Given the consistency of the nucleus electric charge, the upper potential energy worth indicates the absence of negative charges, which might mean that there are fewer electrons during this region. Therefore a high electrostatic potential indicates the relative absence of electrons while low electrostatic potential indicates an abundance of electrons. To accurately analyze the charge distribution of a molecule, a really great quantity of electrostatic potential energy values should be calculated (LibreTexts, 2017). The most effective way to convey this knowledge is to visually represent it, as electrostatic potential map (LibreTexts, 2017). The red regions of the surfaces are the lowest electrostatic potential energy while the blue region is the highest.

Electrostatic potential surfaces are valuable in computer-aided drug design because they assist in understanding electrostatic interactions between the macromolecule and the drug (Otuokere and Amaku, 2015; Otuokere and Alisa, 2014; Cramer and Truhlar, 1992; Igwe et al., 2015). These surfaces can be used to compare different inhibitors with substrates. Electrostatic potential surfaces will be either displayed as isocontour surfaces or mapped onto the molecular negatron density. The shape of a molecule is decided by the negatron density of the molecule (LibreTexts, 2017). The minimum energy was calculated after geometry optimization. The geometry convergence curves are shown in Figures 10 and 11. The geometry optimized energy for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid are -106.5332069610 and -157.470270 au respectively. These are the best feasible position for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid to act as acidifier and acidulant.

Khalida et al., 2012 reported the conformational analysis and geometry optimization of Prasugrel as P2Y12 receptor antagonist. Conformational analysis and geometry optimization of Prasugrel was performed according to Hartree-Fock calculation method using Arguslab software. Their results indicated that the best conformation of the molecule is -99561.2642 kcal/mol. At this point, the molecule will be more active as P2Y12 receptor antagonist and reduce platelets aggregation more effectively (Khalida et al., 2012). Amaku and Otuokere, (2015) reported the conformational analysis of a potent anticancer drug 3-(4-amino-1-oxo-1,3-dihydro-H-

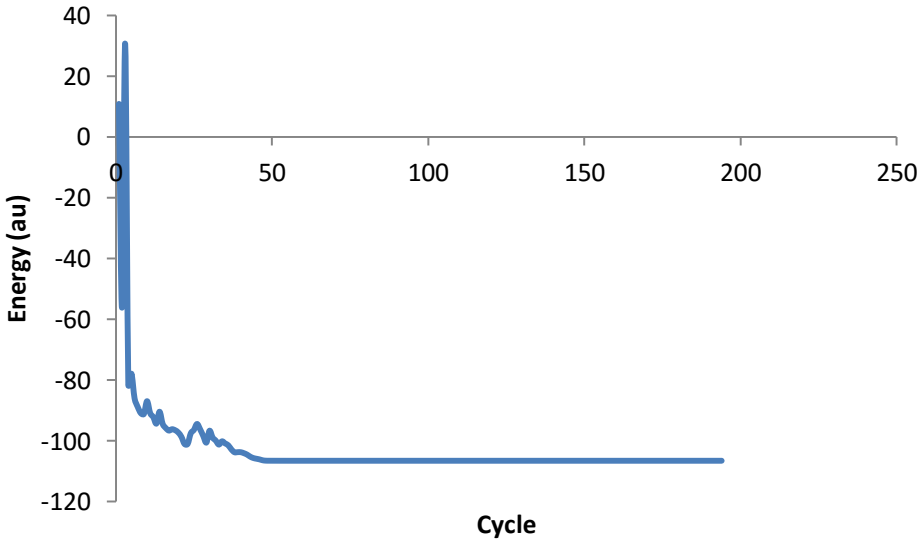

Figure 10. Geometry convergence curve of hexadecanoic acid ethyl ester.

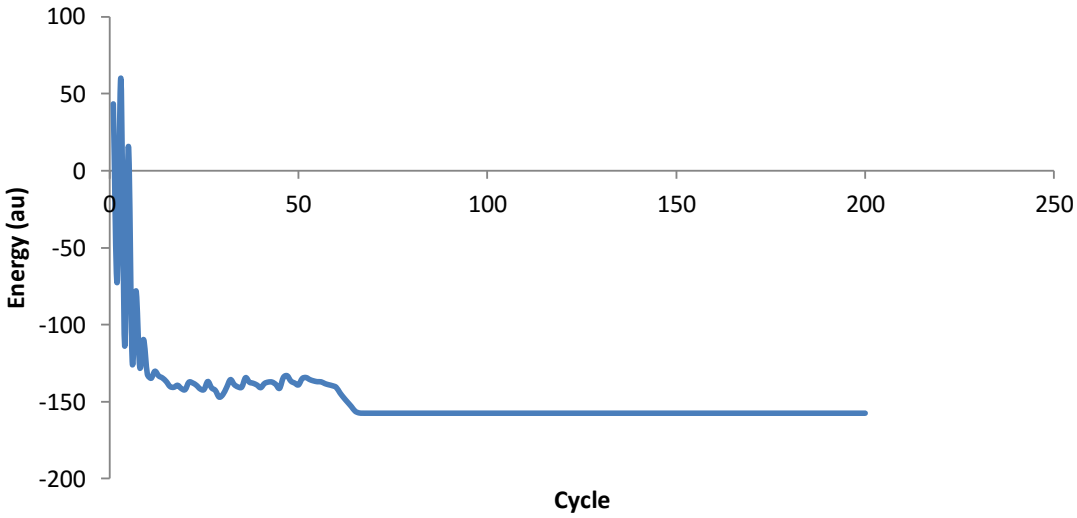

Figure 11. Geometry convergence curve of 10,12- Nonacosadiynoic acid.

isoindol-2-yl) Piperidine-2,6-Dione (Lenalidomide). Conformational analysis and geometry optimization of lenalidomide was performed according to the Hartree-Fock (HF) calculation method by ArgusLab 4.0.1 software. The minimum heat of formation was calculated by geometry convergence function by ArgusLab software. The most feasible position for the drug to interact with the receptor was found to be -23.107576 au (-14500.236400 kcal/mol).

Conclusion

Hexadecanoic acid ethyl ester and 10,12- nonacosadiynoic acid have been reported to be acidifier, acidulant and arachidonic acid inhibitor (Duke,1996). Acidifiers are chemicals that reduce the pH of the body. They help in food digestion in patients suffering from achlorhydria. These patients are not able to secret HCl for food digestion. These compounds may be beneficial since they increase gastric acid when ingested.

The geometry optimized energy for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid are -106.5332069610 and -157.470270 au respectively. These are the best feasible position for hexadecanoic acid ethyl ester and 10,12-nonacosadiynoic acid to act as acidifier and acidulant.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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