DESIGNING OF NANOCOMPOSITE MODEL STRUCTURE USING GLYCITEIN AND GENISTEIN WITH TWELVE DIFFERENT METAL ATOMS USING IN SILICO METHOD

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ABSTRACT

Nanocomposite formulation is still in its evolving state. However due to its significant therapeutic applications it has grabbed the attention of many researchers. Isoflavone which is widely found in soy products have tremendous medicinal properties when it interacts with nanoparticles can become a boon. Hence in this study, we are reporting the interaction properties/patterns of two ubiquitous flavones namely Glycitein and Genistein forming a nanocomposite model with 12 different metals such as Gold, Silver, Palladium, Platinum, Ruthenium, Rhodium, Cadmium, Iron, Nickel, Zinc, Copper and Antimony based on their potency to form nanoparticles. To mimic the Nanocomposite, model the formulation was conducted in Avogadro Software for windows. Glycitein and Genistein create a possibility of selecting the most suitable -OH position that would serve as the binding site. On selection of the appropriate binding site the interaction amid two molecules of glycitein and genistein placed sidewise held together by above-mentioned metals also surrounded by the same metal on another vacant -OH position forming a close saturated structure subjected for interaction. Based on predominantly energy levels the least energy obtained model was Cadmium and the peak procured by Antimony making it least stable and unfavorable for the perceived result.

Keywords: Isoflavone, Nanoparticle, Glycitein, Genistein, and Avogadro software

1. INTRODUCTION

Over the years, science and technology have opened wide doors for various new subjects. In this regard research is one such pillar that has forced people to look beyond the decision boundaries. One such subject that is evolving is nanoparticle technology. Though it appears to be tiny, it can play a pivotal role in tending various medical applications. In this context scientists after arranging their fundamentals had led to findings of Nanoparticle mediated drug delivery. Nanoparticles are defined as solid particles with sizes ranging from 10nm - 100nm. They are basically two types of nanoparticles [Jong and Borm (2008)]; polymeric [Crucho and Barros (2017)], that entrap drug molecules inside their core [Vrignaud et al. (2011)] and metallic [Venkatesh et al. (2018)], that attach the drug molecule directly on the surface [Levin et al. (2009)]. Although our focus stays on the latter one as it seems to be a more oriented one towards recovering from various ailments. The metals selected here are based on their potency to form nanocomposite structures and also used in therapeutic applications namely...
gold (Au) [Duncan et al. (2010)], silver (Ag) [Dos Santos et al. (2014)], palladium (Pd) [Adams et al. (2014)], platinum (Pt) [Kim et al. (2010)], ruthenium (Ru) [Viauet al. (2003)], rhodium (Rh) [Xu et al. (2019)], cadmium (Cd) [Qi et al. (2001)], iron (Fe) [Mahdy et al. (2012)], nickel (Ni) [Guo et al. (2009)], zinc (Zn) [Rojas et al. (2016)], copper (Cu) [Kruk et al. (2015)], and antimony (Sb) [Yin et al. (2019)].

Isoflavone – polyphenolic compounds naturally occurring can predominantly be found in various food supplements, exemplary in soy products and legumes [Thrane et al. (2017)]. They can be a helping aid in treating various serious conditions like type II diabetes mellitus [Pabich and Materska (2019)], cardiovascular diseases [Thangavel et al. (2019)], cholesterol-reducing [Lu et al. (2019)], or in chemotherapeutics [Spagnuolo et al. (2015)] and used as strong antioxidants [Shimoda and Hamada (2010)]. The isoflavone being phytoestrogen also plays an effective role in alleviating women’s menstrual problems [Thangavel et al. (2019)]. Based on all this groundwork’s we select Glycitein, as one of the active components of soy products exhibiting exceptional results in biological and estrogenic activity mainly due to its chemical forms in which it exists [Vitale et al. (2013)] and also Genistein which is used as an angiogenesis inhibitor [Suet al. (2005)]. Hence, the isoflavone glycitein and genistein can become a prime source to study its interactions in association with the above-mentioned 12 metals.

2. MATERIALS AND METHODS:

Since a nanoparticle consists of several metal atoms when synthesized, hence, for the representation of the same, we consider a single metal atom for its interaction with the isoflavone. To study the inter-relationship amid the considered isoflavone and the metal atom, both glycitein and genistein structures constructed in the Avogadro software [Hanwell et al. (2012)] were subjected to energy optimization. Glycitein has 2 - OH groups present at the 7 and 4' position whereas genistein has 3 – OH groups at the 4', 5, and 7 position respectively. To ensure the susceptible position where energy-optimization could be the least. So, metal atoms were added in their respective binding sites and the least one was to be selected. The 12 metals were selected in terms of their capability to form nanocomposite structures and also their applications in therapeutics, those are namely: gold (Au) [Duncan et al. (2010)], silver (Ag) [Dos Santos et al. (2014)], palladium (Pd) [Adams et al. (2014)], platinum (Pt) [Kim et al. (2010)], ruthenium (Ru) [Viauet al. (2003)], rhodium (Rh) [Xu et al. (2019)], cadmium (Cd) [Qi et al. (2001)], iron (Fe) [Mahdy et al. (2012)], nickel (Ni) [Guo et al. (2009)], zinc (Zn) [Rojas et al. (2016)], copper (Cu) [Kruk et al. (2015)], and antimony (Sb) [Yin et al. (2019)]. The 4’ OH of glycitein and 5 OH of genistein were observed to be the most suitable ones. Therefore, the -OH groups present at the 4’ and 5 positions were replaced by a metal atom one at a time. In this study, we are trying to report two of the same drug molecules interacting with the metal atom. Precisely, a metal settled in between with a glycitein or genistein molecule situated sidewise along with the same metal being placed at other OH positions. On that account, the entire setup could be metals attached altogether to provide a circumference for the drug interaction. On completion of the entire build up the energy optimization was monitored along with the bond angle and bond length (O-R-Metal-OL) were reported below.
3. RESULTS AND DISCUSSION

Interaction of Glycitein with a metal nanoparticle

The structure of Glycitine was made using Avogadro software as shown in Figure 1 with its chemical structure, where the energy was found to be 244.853 KJ/Mol. The molecule consists of three benzene rings associated with 2 - OH groups serving as metal binding sites, present at the 7ortho position of A ring (Figure 2A) and 4’ meta position of B ring (Figure 2B). To be noted, that single drug molecule of glycitein when -OH was replaced at the 7 positions and the energy was found to be 241.785 KJ/Mol after energy optimization it was found to be little less in comparison with the 4’ binding site that is 242.785 KJ/Mol.

![Figure 1](image1.png)

**Figure 1** A) Chemical structure of glycitein, B) Structure of glycitein formulated using Avogadro software

![Figure 2](image2.png)

**Figure 2** Structure of Glycitein molecule with metal at -OH position A) Cd metal at 7 OH position, B) Cd metal at 4’ OH position

But, when the interaction took place amid 2 glycitein molecules and a metal atom is forming the bridge, surprisingly the 4’ site was found to be more susceptible than 7 position. For instance, the energy level for cadmium at 4’OH was 461.132 KJ/Mol and at the 7 OH position it was found to be 463.43 KJ/Mol. One of the reasons for the selection of cadmium metal in order to find the most suitable binding site is due to the previous studies conducted in the same software where we found cadmium gives the least energy after optimization against other metals [27]. Once sure of the destined position then, the drug molecules together bonded with the above-mentioned metal atoms at the 4’ meta-position and were subjected to energy optimization, one followed by the other. While monitoring the energy levels when the central metal atom was holding the two glycitein molecules, followed by the
addition of twin metal atoms on either 7-position seemed to be decreasing hence it can be said on the addition of metals, the setups energy was minimizing.

On reaching its threshold where the structure was quite stable, the optimized energy of cadmium metal was found to be least about 461.132 KJ/Mol (Figure 3 G) with Platinum slightly greater than around 461.222 KJ/Mol (Figure 3 D) in comparison to the other 12 metals; On contrary, antimony was at its peak whose energy was when calculated gave a value of 519.92 KJ/Mol as depicted in Figure 3L. The figures mentioned below can give a wider view followed by (Table 1) stating all the respective molecules: energies, bond angle and bond length.

![Figure 3 Nanocomposite model structure of glycitein with A) Gold (Au_Gy), B) Silver (Ag_Gy), C) Palladium (Pd_Gy), D) Platinum (Pt_Gy), E) Ruthenium (Ru_Gy), F) Rhodium (Rh_Gy), G) Cadmium (Cd_Gy), H) Iron (Fe_Gy), I) Nickel (Ni_Gy), J) Zinc (Zn_Gy), K) Copper (Cu_Gy), L) Antimony (Sb_Gy).](image)

| Metal       | Compound name | Energy (KJ/Mol) | Bond Angle (°) | Bond Length |
|-------------|---------------|----------------|----------------|-------------|
| Gold        | Au_Gy         | 467.252        | 89.9°          | 1.859 Å     |
| Silver      | Ag_Gy         | 471.191        | 176.0°         | 1.973 Å     |
| Palladium   | Pd_Gy         | 462.551        | 89.8°          | 1.914 Å     |
| Platinum    | Pt_Gy         | 461.222        | 89.8°          | 1.955 Å     |
| Ruthenium   | Ru_Gy         | 468.343        | 174.1°         | 2.018 Å     |
| Rhodium     | Rh_Gy         | 470.587        | 175.0°         | 1.896 Å     |

*Figure 3 Nanocomposite model structure of glycitein with A) Gold (Au_Gy), B) Silver (Ag_Gy), C) Palladium (Pd_Gy), D) Platinum (Pt_Gy), E) Ruthenium (Ru_Gy), F) Rhodium (Rh_Gy), G) Cadmium (Cd_Gy), H) Iron (Fe_Gy), I) Nickel (Ni_Gy), J) Zinc (Zn_Gy), K) Copper (Cu_Gy), L) Antimony (Sb_Gy).*
Designing of Nanocomposite model structure using Glycitein and Genistein with twelve different metal atoms using in silico method

| Metal | Symbol | Code  | Energy (KJ/Mol) | Angle (°) | Bond Length (Å) |
|-------|--------|-------|----------------|----------|-----------------|
| Cadmium | Cd_Gy | 461.132 | 109.0° | 2.000 Å | 2.000 Å |
| Iron | Fe_Gy | 471.911 | 174.3° | 1.891 Å | 1.891 Å |
| Nickel | Ni_Gy | 463.208 | 90.0° | 1.749 Å | 1.749 Å |
| Zinc | Zn_Gy | 462.135 | 108.9° | 1.795 Å | 1.795 Å |
| Copper | Cu_Gy | 468.417 | 108.7° | 1.874 Å | 1.874 Å |
| Antimony | Sb_Gy | 519.924 | 91.5° | 2.014 Å | 2.014 Å |

Interaction of Genistein with a metal nanoparticle

Genistein molecule consists of three benzene rings. A structure of Genistein was made with the help of Avogadro software, shown in Figure 4 (A). The energy level was calculated through Avogadro software was then found to be 237.654 KJ/Mol. The molecule has three OH groups, two of them are present in the A ring and one in the C ring which serve as positions for binding of metals. In the A ring, the OH groups are present at the Para position (5 positions) and Meta position (7 positions). In the C ring, the -OH group is present at the ortho position (4’ position).

The metals selected for this study are widely used to form nanoparticles for applications in therapeutics. The metal atoms were attached to each of the OH groups of the molecule and the energies at each site were found to be different. Energy of the molecule when interacted with the OH of the Para position was found to be 232.975 KJ/Mol. Similarly, the energies of the molecule when interacted with the OH groups at Meta and Ortho position respectively were 233.184 KJ/Mol and 233.197 KJ/Mol.
The -OH at the Para position (5 position) after being interacted with metal atoms was found to be the most stable site for attaching two drug molecules through a metal atom. Thus, 12 nanocomposite structures were formed when drug molecules interacted with metals. It was also observed that a free Genistein molecule without any metal had more energy. As the metal atoms were being simultaneously added to the drug molecule the energy kept on decreasing. After the complete optimization of energy, the final energy was noted in a table (Table 2). From the table, it can be observed that Genistein, when reacted with Cadmium, had the least energy and had maximum energy when interacting with Antimony.

Figure 6 Nanocomposite model structure of metals with A) Gold (Au), B) Silver (Ag), C) Palladium (Pd), D) Platinum (Pt), E) Ruthenium (Ru), F) Rhodium, G) Cadmium (Cd), H) Iron (Fe), I) Nickel (Ni), J) Zinc (Zn), K) Copper (Cu), L) Antimony (Sb).

Table 2 List of energy levels for different metal-Genistein nanocomposite particles with bond angle and bond lengths.

| Metal    | Compound name | Energy (KJ/Mol) | Bond Angle (°) | Bond Length |
|----------|---------------|-----------------|----------------|-------------|
|          |               |                 | O_L-Metal-O_R  |             |
|          |               |                 | O_L-Metal       | Metal-O_R   |
| Gold     | Au_Gy         | 457.117         | 178.5          | 1.862 Å     | 1.862 Å     |
| Silver   | Ag_Gy         | 449.572         | 176.0°         | 1.969 Å     | 1.969 Å     |
| Palladium| Pd_Gy         | 449.202         | 89.8°          | 1.915 Å     | 1.915 Å     |
| Platinum | Pt_Gy         | 445.259         | 89.8°          | 1.957 Å     | 1.957 Å     |
| Ruthenium| Ru_Gy         | 445.691         | 174.1°         | 2.016 Å     | 2.016 Å     |
| Rhodium  | Rh_Gy         | 448.646         | 175.0°         | 1.895 Å     | 1.895 Å     |
| Cadmium  | Cd_Gy         | 430.015         | 109.0°         | 2.004 Å     | 2.004 Å     |
| Iron     | Fe_Gy         | 452.493         | 174.3°         | 1.887 Å     | 1.887 Å     |
4. CONCLUSION

In glycitein molecules, the OH group present at 4’ meta-position could be best suitable to be acting as a binding site for forming the bond amid two twin glycitein molecules. Whereas in case of genistein 5 Para position was found to be the appropriate one with the least energy-optimization against both 4’ Meta and 7 ortho position -OH groups. The presence of –CH3 group in glycitin molecule may be the cause for this phenomenon. Supplementary to this on the addition of metals on the other sites excluding meta-position for glycitein and Para-position for genistein the energy was slowly depleting which could be encountered very well in the energy levels of two-drug molecules. In consideration of all, from the above observation cadmium metal was found to be forming the most stable nanocomposite structure with least energy in comparison to other selected metals, among them antimony being least stable in case of both the isoflavones.

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