ISSN: 2287-688X

Annals of
Plant Sciences

Volume 11, Issue 01 (2022) pp. 4621-4627

Research Article

Computational Designing of Trimolecular Nanocomposite Model Structure of Gallic Acid with Different Metals

Deepsikha Chatterjee, Oindrela Ganguly, Debraj Hazra and Rajat Pal

Department of Microbiology and Biotechnology, Sister Nivedita University Kolkata – 700156, India

Abstract

Bioflavonoids are defined as the chemical compounds with lower molecular weight, obtained from plants and other natural derivatives which can be applied in synthesizing various drugs in the field of therapeutic medicine. Due to the metabolism in human body there is a requirement of a vehicle that can carry the drugs to different parts of the body, and help in increasing the retention of drugs in the system for better effectiveness. The vehicles used are termed as nanoparticles, which have become an important aspect of medical science. In order to understand the drug and nanoparticle interaction, we selected Gallic acid as a drug molecule for having various beneficial properties as a therapeutic drug and can easily interact with the metal atoms. We considered eleven metals in order to construct the closed nanocomposite structures by using the Avogadro software. After the construction of the structures, they were subjected to energy minimization for obtaining the most stable structures. After formulating all the nanocomposite structures, zinc (Zn) was found to have the lowest energy value. Hence this metal has been considered as the most suitable for interaction with Gallic acid. It was also observed that –OH group at the meta- position of the Gallic acid is the best site for metal atom attachment.

Keywords: *Bioflavonoids, drug-delivery, nanocomposite, Avogadro.*

Introduction

The series of development in the field of science and technology has played a vital role in shaping the human civilization and advancements we see today. Similarly, the health care system has also been benefited by the technological development. A comparatively recent study of the nanoparticles has established itself as the center of attention for many researchers. Nanoparticle-mediated drug delivery has also become a topic of discussion and found to be of vast application to combat various ailments. Nanoparticles can be classified into two (Jong & Borm. 2008), namely; the metallic nanoparticles(Kumar. *et al.*, 2018) are the ones which have drug molecules attached to its surface(Levin. *et al.*, 2009) and the polymeric nanoparticles (Crucho & Barros. 2017), are the ones where the drug molecules are trapped within the core (Vrignaud. *et al.*, 2011). The metallic nanoparticles are the most widely used due to their structure containing drug molecules on their surface which is effective against various diseases. A series of metals have been discovered which has the capability to synthesize nanoparticles, such as iron (Fe) (Mahdy. *et al.*, 2012), copper (Cu) Kruk. *et al.*, 2015, gold (Au) (Duncan. *et al.*, 2010), silver (Ag) (Santos. *et al.*, 2014), platinum (Pt) (Kim. *et al.*, 2010), palladium (Pd) (Adams. *et al.*, 2014), zinc (Zn) (Rojas. *et al.*, 2016), cadmium (Cd) (Qi. *et al.*, 2001), rhodium (Rh) (Zu. *et al.*, 2019), ruthenium (Ru) (Viau. *et al.*, 2003), antimony (Sb) (Yin. *et al.*, 2019).

Flavonoids are the polyphenolic compounds of lower molecular weight obtained from various plant derivatives. Flavonoids are widely used as antioxidants (Anjaneyulu &

***Corresponding Author:**
Rajat Pal;

DOI: http://dx.doi.org/10.21746/aps.2022.11.01.11

Chopra. 2004), which reduce the oxidative stress caused by the reactive oxygen species and is vital for the treatment of cardiovascular diseases (Geleijnse. *et al.*, 2008), they are also used as anti-inflammatory (Guardia. *et al.*, 2001), anti-thrombotic (Vazhappilly. *et al.*, 2019) and anti-cancer (Ren. *et al.*, 2003) agents. In this paper we have discussed about Gallic acid, as it has its application at a wider spectrum. This research article is a study of the interaction of Gallic acid and the eleven metals (Fe, Cu, Au, Ag, Pt, Pd, Zn, Cd, Rh, Ru, and Sb). Therefore, our study will aid the selection of the most suitable metal in order to synthesize nanoparticles.

Methods

To study the interaction between metal nanoparticles and the drug molecules, we began with constructing the structure of Gallic acid in Avogadro software for windows (Hanwell. *et al.*, 2012). Gallic acid has three binding sites at its three -OH groups. All these three –OH groups are eligible to bind with the nanoparticles. However, the two –OH groups at the meta-positions have the lowest energy values, making them stable in nature (Hazra & Pal. 2020). The constructed structure of Gallic acid is shown in figure 1B.

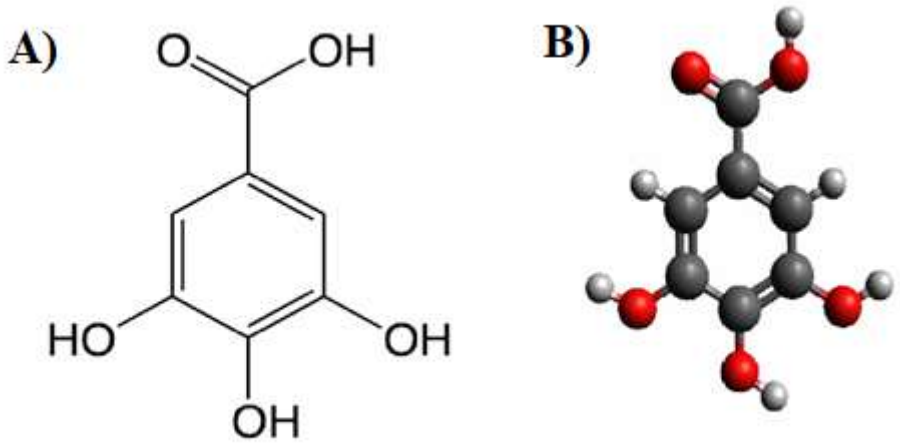

Figure 1: Diagrammatic chemical structure of Gallic acid (A) and Avogadro software-generated structure of Gallic acid (B).

To the best of our knowledge, a single nanoparticle contains multiple metal atoms, which is not possible to mimic *in silico*. So, for our convenience we selected a single metal atom to study the interaction between drug and metal atom. The metals, Copper (Cu), Gold (Au), Silver (Ag), Iron (Fe), Zinc (Zn), Ruthenium (Ru), Antimony (Sb), Palladium (Pd), Platinum (Pt), Rhodium (Rh) and Cadmium (Cd) have been chosen as per their potentiality towards the synthesis of a nanoparticle complex for the application in drug delivery. We made three Gallic acid structures interact with three metal atoms in each one of their meta- positions in such a way that it forms a single closed nanocomposite structure. In this case, a metal atom connects two Gallic acid structures by replacing two hydrogen atoms at a time from their meta- positions bridging the gap between the two oxygen atoms. After completion of structures, the energy was minimized. Along with energy levels, O–metal bond length, C–O and C–O–metal bond angles were also measured in each of the positions the metal atom is present. We list all these parameters in tabular form (Table 1 and 2). From the lowest energy level, the most stable structure and susceptible position for nanoparticle binding were in view.

Results and Discussions

Gallic acid has three metal atom binding sites, two –OH groups at the meta- positions and

one at the para- position. As have already been discussed, Cu, Au, Ag, Zn, Pt, Pd, Ru, Sb, Rh and Cd (Hazra & Pal. 2020; Hazra. *et al.*, 2020), when interacted with Gallic acid structure at their meta- binding site show minimum energy as compared to their para- binding site. Although iron (Fe), deviates a bit and possess a lesser energy at para- position compared to the meta- binding site when made to interact with Gallic acid model structure, the difference in energy is found to be negligible. So, we have avoided choosing the para- position of gallic acid as a binding site whilst considering formulating a closed nanocomposite model with drug-metal interaction.

To our convenience, in these model nanocomposites we have marked each of the metal atom: alphabetically and each oxygen atom: numerically. A reference structure of the same has been depicted in figure 2.

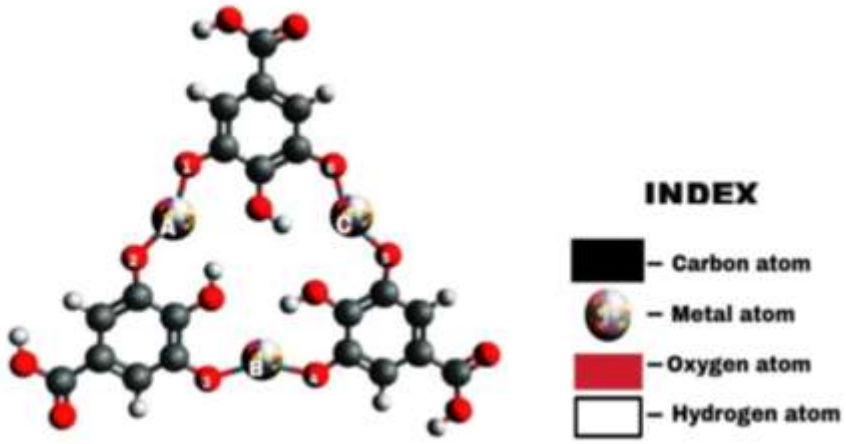

Figure 2: Schematic diagram for the reference of the positions of metals (labeled alphabetically) and oxygen atoms (labeled numerically) for calculating bond length and bond angle in each nano-model.

So, we created virtual models with three Gallic acid molecules at a time and attaching them with three metal atoms in the manner that has been mentioned in the earlier section. After energy minimization of these closed structures, we have listed down all their respective values in Table 1 and depicted the resultant nanoparticle nanocomposite models in Figure 3. Furthermore, we have designated the metal-oxygen arranging these metals according to their atomic mass, we find variations in energy values from as low as an energy gap of approx. 3 KJ/mole going as high as an energy gap of approx. 113 KJ/mole. With these 11 metals, we found Zinc (Zn) to possess the minimum energy value compared to the rest whereas Platinum (Pt) indicated to the possession of the highest energy value in the chart. The parameters are listed in Table1.

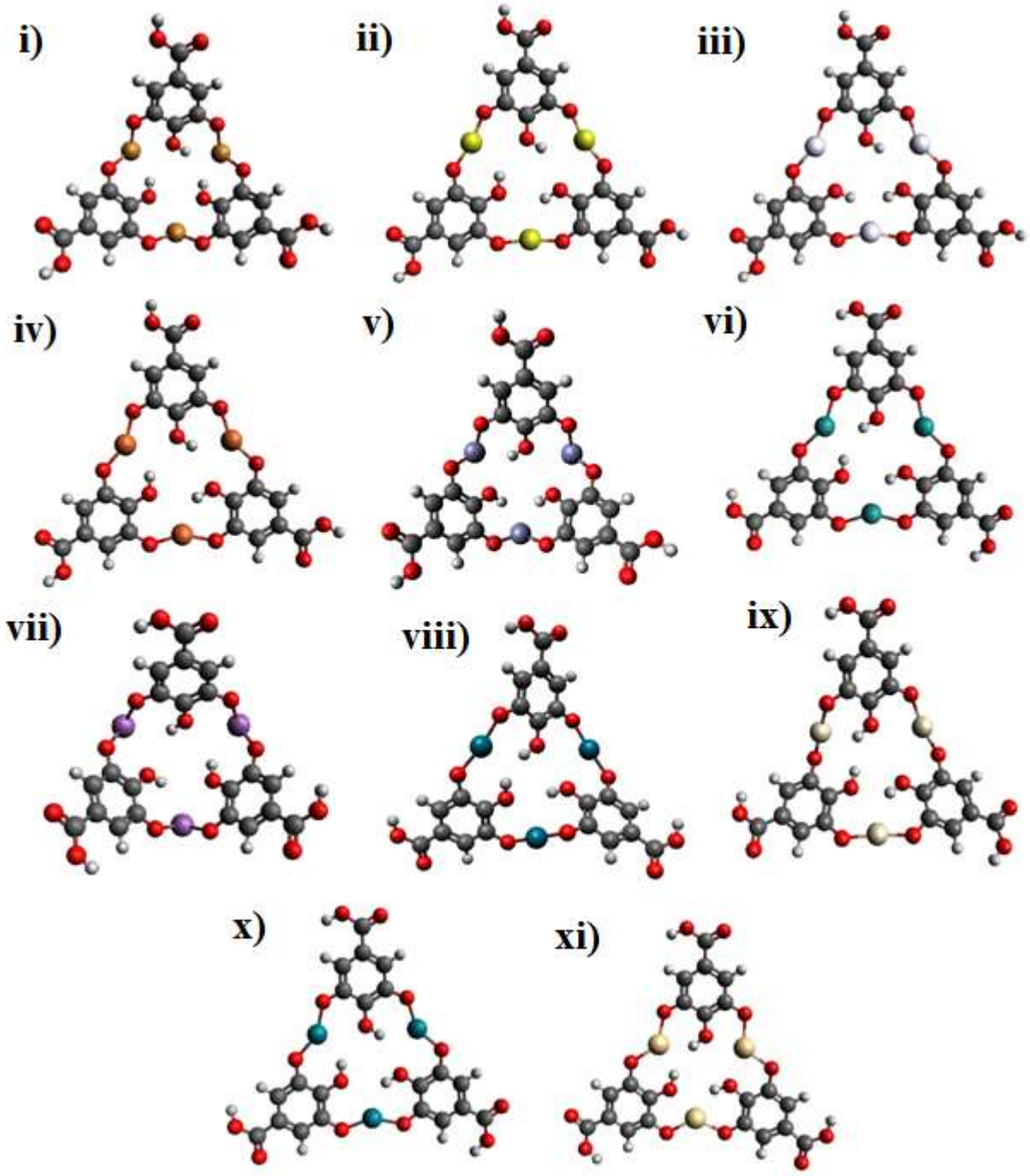

Figure 3: Nanocomposite model structures of Gallic acid with (i) Copper, (ii) Gold, (iii) Silver, (iv) Iron, (v) Zinc, (vi) Ruthenium, (vii) Antimony, (viii) Palladium, (ix) Platinum, (x) Rhodium, (xi)Cadmium

There have been reports of the formulation of nanocomposites with Gallic acid using gold (Moreno-Alvarez. *et al.*, 2010), silver (Ghodake*et. al.*, 2020; Lakshmipathy & Nanda. 2015; Farrokhnia. *et al.*, 2019), palladium (Can. *et al.*, 2012)and iron (Zeng. *et al.*, 2016) However an in-depth study in this matter of drug-metal interaction has yet not been elucidated.

Table 1: List of energy levels of all Gallic acid – nanoparticle nanocomposite model structures along with O-Metal-O bond angles.

Compound	Metal	Energy	Bond Angle (O-M-O)

No.		(KJ/mol)	(Positions for Oxygen-Metal-Oxygen bond have been referred from Fig.2)		
			1-A-2	3-B-4	5-C-6
(i)	COPPER	262.518	108.2	108.5	108.4
(ii)	GOLD	538.757	169.1	169.1	169.1
(iii)	SILVER	375.95	154.5	155.8	155.5
(iv)	IRON	404.616	152.2	152.2	152.2
(v)	ZINC	249.648	108.5	108.4	108.6
(vi)	RUTHENIUM	438.066	149.0	148.4	147.3
(vii)	ANTIMONY	492.509	91.2	91.2	91.2
(viii)	PALLADIUM	517.404	170.4	172.3	180.0
(ix)	PLATINUM	551.655	179.8	170.7	167.9
(x)	RHODIUM	466.98	148.9	148.9	148.9
(xi)	CADMIUM	401.559	132.5	126.0	126.1

For clarity, we have charted down the bond lengths with the corresponding metal and oxygen positions in Table 2.

Bond Length:
(Positions for Oxygen-Metal bond in the table have been referred from Fig.2)

Table 2: List of all Gallic acid – nanoparticle nanocomposite model structures with O-metal bond lengths at different positions.

Compound No.	Metal	Bond Length (O-M)					
		1-A	2-A	3-B	4-B	5-C	6-C
(i)	COPPER	1.876	1.878	1.879	1.880	1.879	1.878
(ii)	GOLD	1.860	1.859	1.860	1.859	1.860	1.859
(iii)	SILVER	1.966	1.968	1.973	1.973	1.969	1.968
(iv)	IRON	1.887	1.888	1.887	1.888	1.887	1.888
(v)	ZINC	1.802	1.800	1.798	1.800	1.801	1.802
(vi)	RUTHENIUM	2.014	2.016	2.019	2.019	2.016	2.015
(vii)	ANTIMONY	2.015	2.017	2.015	2.017	2.015	2.017
(viii)	PALLADIUM	1.931	1.929	1.922	1.922	1.914	1.912
(ix)	PLATINUM	1.969	1.969	1.968	1.969	1.961	1.960
(x)	RHODIUM	1.895	1.896	1.895	1.896	1.895	1.896
(xi)	CADMIUM	2.001	2.041	2.009	1.990	2.008	2.043

Conclusion

In Gallic acid, the formation of the closed composite structures with various metals provide us with a series of different energy values, which can be used as a reference by the research groups working on the metal nanoparticle formation used for drug delivery.

As per our observations and the energy values obtained, zinc (zn) has the lowest energy after interacting with Gallic acid and platinum (Pt) tends to be the highest. These results clearly justify that zinc (Zn) is the most appropriate metal atom that can be used to construct the metal nanoparticle with Gallic acid.

References

1. De Jong, W. H. and Paul, J. B. "Drug delivery and nanoparticles: applications and hazards." *International journal of nanomedicine* 3.2 (2008): 133 – 149.
2. Kumar, H. K., Nagasamy, V., Himangshu, B. and Anuttam, K. "Metallic nanoparticle: a review." *Biomedical Journal of Scientific & Technical Research* 4.2 (2018): 3765-3775.
3. Levin, C. S., Cristina, H., Tamer, A. A., Anna, T. K., Emilia, M., Peter, N., Kenton, H. Naomi, J. H. "Magnetic− plasmonic

core− shell nanoparticles." *ACS nano* 3.6 (2009): 1379-1388.
4. Crucho, C. I. and Maria, T. B. "Polymeric nanoparticles: A study on the preparation variables and characterization methods." *Materials Science and Engineering: C* 80 (2017): 771-784.
5. Vrignaud, S., Jean, P. B. and Patrick, S. "Strategies for the nanoencapsulation of hydrophilic molecules in polymer-based nanoparticles." *Biomaterials* 32.33 (2011): 8593-8604.
6. Mahdy, S. A., Qusay, J. R. and Kalaichelvan, P. T. "Antimicrobial activity of zerovalent iron nanoparticles." *International Journal of Modern Engineering Research* 2.1 (2012): 578-581.
7. Kruk, T., Krzysztof, S., Joanna, S., Robert, P. S. and Piotr, W. Synthesis and antimicrobial activity of monodisperse copper nanoparticles. Colloids and Surfaces B: Biointerfaces, 128.1(2015): 17 – 22.
8. Duncan, B., Chaekyu, K. and Vincent, M. R. "Gold nanoparticle platforms as drug and biomacromolecule delivery systems." *Journal of controlled release* 148.1 (2010): 122-127.
9. Santos, D., Carolina, A., Marcelo, M. S., Avinash, P. I., Indarchand, G., Stefania, G., Massimiliano, G., Aniket, G. and Mahendra Rai. "Silver nanoparticles: therapeutical uses, toxicity, and safety issues." *Journal of pharmaceutical sciences* 103.7 (2014): 1931-1944.
10. Kim, J., Takuji, S. and Yusei, M. "The effect of TAT conjugated platinum nanoparticles on lifespan in a nematode Caenorhabditis elegans model." *Biomaterials* 31.22 (2010): 5849-5854.
11. Adams, C. P., Katherine, A. W., Sherine, O. O., Kathryn, M. D. Size-Dependent Antimicrobial Effects of Novel Palladium Nanoparticles. PLoS ONE, 9.1 (2014): e85981.
12. Rojas, S., Francisco, J. C., Carmen, R. M., Patricia, H., Tania, H., Christian, S., Jorge, A. N. and Elisa, B. "Nanoscaled zinc pyrazolate metal–organic frameworks as drug-delivery systems." *Inorganic chemistry* 55.5 (2016): 2650-2663.
13. Qi, L., Helmut, C. and Markus, A. "Synthesis and characterization of CdS nanoparticles stabilized by double-hydrophilic block copolymers." *Nano Letters* 1.2 (2001): 61-65.
14. Xu, L., Danye, L., Dong, C., Hui, L. and Jun, Y. "Size and shape controlled synthesis of rhodium nanoparticles." *Heliyon* 5.1 (2019): e01165.
15. Yin, W., Wenwen, C., Ke, W., Wenkai, Y., Yichuan, R. and Bohejin, T. "Facile synthesis of Sb nanoparticles anchored on reduced graphene oxides as excellent anode materials for lithium-ion batteries." *Journal of Alloys and Compounds* 797 (2019): 1249-1257.
16. Anjaneyulu, M. and Kanwaljit, C. "Quercetin, an anti-oxidant bioflavonoid, attenuates diabetic nephropathy in rats." *Clinical and Experimental pharmacology and physiology* 31.4 (2004): 244-248.
17. Geleijnse, J, M., Peter, C. H. H. "Flavonoids and cardiovascular health: which compounds, what mechanisms?." *The American journal of clinical nutrition* 88.1 (2008): 12-13.
18. Guardia, T., Alejandra, E. R., Americo, O. J. and Lilian, E. P. "Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rat." *Il farmaco* 56.9 (2001): 683-687.
19. Vazhappilly, C. G., Shabbir, A. A., Rula, A. J., Aya, M. A. A., Wafaa, S. R., Varsha, M., Rawad, H., Siddiqui, S. S., Merheb, M., Matar, R., Radhakrishnan, R. "Role of flavonoids in thrombotic, cardiovascular, and inflammatory diseases." *Inflammopharmacology* 27.5 (2019): 863-869.
20. Ren, W., Zhenhua, Q., Hongwei, W., Lei, Z. and Li, Z. Flavonoids: Promising anticancer agents. Medicinal Research Reviews, 23.4 (2003): 519 – 534.
21. Hanwell, M. D., Donald, E. C., David, C. L., Tim, V., Eva, Z., Geoffrey, R. H. "Avogadro: an advanced semantic chemical editor, visualization, and analysis platform." *Journal of cheminformatics* 4.1 (2012): 1-17.
22. Hazra, D. and R. Pal. "Formulation of Metal Nanocomposite model structures with gallic acid and ellagic acid by com-

putational methods." *International Journal of Creative Research Thoughts* 8(2020): 3147-3153.
23. Hazra, D., Doyel, C. and Rajat, P. "Designing of Nanocompositemodel structure using Gallic acid and Ellagic acid with four different metals." *Int. J. of. Life Sciences* 8.3 (2020): 556-562.
24. Moreno-Alvarez, S. A., Martinez-Castanon, G. A., N. Nino-Martinez., Reyes-Macias, J. F., N. Patino-Marin., Loyola-Rodriguez, J. P. and Facundo, R. "Preparation and bactericide activity of gallic acid stabilized gold nanoparticles." *Journal of Nanoparticle Research* 12.8 (2010): 2741-2746.
25. Ghodake, G., Surendra, S., Avinash, K., Rijuta, G. S., Ganesh. D. S., Asad, S., Omar, S. and Dae, Y. K. "Gallic acid-functionalized silver nanoparticles as colorimetric and spectrophotometric probe for detection of Al3+ in aqueous medium." *Journal of Industrial and Engineering Chemistry* 82 (2020): 243-253.
26. Lakshmipathy, M. and Anima, N. "Assessment of in vitro prophylactic efficacy of gallic acid fabricated silver nanoparticles." *J. Chem. Pharm. Res* 7 (2015): 356-361.
27. Farrokhnia, M., Sadegh, K. and Sahar, A. "Strong hydrogen bonding of gallic acid during synthesis of an efficient AgNPs colorimetric sensor for melamine detection via dis-synthesis strategy." *ACS Sustainable Chemistry & Engineering* 7.7 (2019): 6672-6684.
28. Can, M., Emrah, B. and Mahmut, O. "Synthesis and characterization of gallic acid resin and its interaction with palladium (II), rhodium (III) chloro complexes." *Industrial & engineering chemistry research* 51.17 (2012): 6052-6063.
29. Zeng, J., Ming, C., Yong, W., Ling, W., Ling, C., Zhen, L., Yongyou, W., Mingyuan, G. and Zhifang, C. "pH-Responsive Fe (III)–Gallic Acid Nanoparticles for In Vivo Photoacoustic-Imaging-Guided Photothermal Therapy." *Advanced healthcare materials* 5.7 (2016): 772-780

Source of support: Nil; **Conflict of interest:** Nil.

Cite this article as:
Chatterjee, D., Oindrela, G., Debraj, H. and Rajat, P. "Computational Designing of Trimolecular Nanocomposite Model Structure of Gallic Acid with Different Metals."" *Annals of Plant Sciences*.11.1 (2022): pp. 4621-4627.

DOI: http://dx.doi.org/10.21746/aps.2022.11.1.11