ISSN: 0975-833X

Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 13, Issue, 05, pp.17585-17589, May, 2021

DOI: https://doi.org/10.24941/ijcr.41494.05.2021

RESEARCH ARTICLE **OPEN ACCESS**

IN SEARCH OF METAL FOR CONSTRUCTION OF METAL – FERULIC ACID NANOCOMPOSITE STRUCTURE BY *IN SILICO* METHOD

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ARTICLE INFO

Article History:
Received 19th February, 2021
Received in revised form
15th March, 2021
Accepted 20th April, 2021
Published online 30th May, 2021

Key Words

Flavonoids, Metal Nanoparticles, Nanocomposite Structures, Avogadro Software.

ABSTRACT

Nanoparticle and drug molecule interaction study has become a very important topic for research which can open various avenues for several biomedical fields. Here we tried to formulate a model nanoparticle structure *in silico* using Avogadro soft ware in several ways. We went up to nine atoms of metals (Zinc, Cadmium and Copper) along with six Boron atoms for the construction of the nanoparticle model structure. We hypothesize that it would be energetically more favourable if Boron atoms get inserted in between the metal atoms during their bond formation rather than metals interacted amongst them directly and Boron atoms are attached at the corner. We also tagged ferulic acid to all three computationally formulated nanoparticles and observed their energy levels. It was found that Zinc and Cadmium are the better choice for synthesizing nanocomposite with ferulic acid rather than Copper.

Citation: Soumalya Chatterjee, Debraj Hazra and Rajat Pal. "In Search of Metal for Construction of Metal – Ferulic acid Nanocomposite Structure by in silico method*", 2021. International Journal of Current Research, 13, (05), 17585-17589.*

INTRODUCTION

Nanoparticle is a small particle that ranges between 1 to 100 nm in size by at least one dimension, undetectable by the human eyes. Nanoparticles can exhibit significantly different physical and chemical properties to their larger material counterparts. More properly we can define a nanoparticle suspension where at least half of the particles in the number size distribution must be of hundred nm or below measurement. Mostly the nanoparticles are made up of few hundreds of atoms. The material's properties change as their size approaches to the atomic scale, this happens due to the increase of surface area to volume ratio. As a result, the material's surface atoms dominate the material performance. Because of their very small size, nanoparticles possess a very large surface area to volume ratio when compared to bulk materials, like powder, plate and sheet etc. This feature enables nanoparticles to show unexpected optical, physical and chemical properties as they are small enough to confine the electrons and produce Quantum effects (TWI, 2021).

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The huge ranges of applications of nanoparticles in various fields have drawn the focus on its research. The area in which nanoparticles has played the most important role is to study on biomedicine and Agriculture (Hazra and Pal, 2020a). Metals are found to be very good ingredient for synthesis of nanoparticles. Many metals have already been reported for being used as precursor for nanoparticle synthesis among them some mostly common are Gold (Au) (Duncan *et al*., 2010), Silver (Ag) (Santos *et al*., 2014), Copper (Cu) (Kruk *et al*., 2015), Iron (Mahdy *et al*., 2012), Zinc (Zn) (Rojas *et al*., 2016), Nickel (Ni) (Guo *et al*., 2009), Platinum (Pt) (Kim *et al*., 2010), Palladium (Pd) (Adams *et al*., 2014), Ruthenium (Ru) (Xu *et al*., 2019), Rhodium (Rh) (Viau *et al*., 2003), cadmium (Cd) (Qi *et al*., 2001) and antimony (Sb) (Yin *et al*., 2019). The nanoparticles produced by these metals are widely used as a vehicle for drug molecules to be administered during the treatment. Benefits and supports of such vehicle make this drug -nanoparticle composites very useful mode of drug delivery system in medical science. Free drug molecules dissociate and metabolize very easily in the body due to the presence of different metabolic pathways. But if these drug molecules are administered with a vehicle like nanoparticle, the slow release will occur in physiological condition and the drug will get more time to show its activity in the body.

Hence the study of interaction between drug molecule and the nanoparticles have become very useful for scientists who are working on drug -nanoparticles composite formulation and their application in various fields. For the treatment against a huge range of diseases, flavonoids stand in a strong position among various biomolecules having medicinal activity. Hence the composite structure of metal nanoparticles with different flavonoid molecules play key role in the field of biomedical research. Flavonoid – coated nanoparticle formulation also serves the purpose in which the drug molecules are attached on the surface of the nanoparticle during their synthesis (Riaz *et al*., 2020). Many reports have been found where the metal nanoparticles are synthesized by using the extracts of different parts of several plants. This method is commonly known as green synthesis (Shafey, 2020).

In this present study, we have selected ferulic acid as a drug molecule. This flavonoid has major array of applications in various fields and can act as antimicrobial (Shi *et al*., 2016) anti-inflammatory (Zhu *et al*., 2014), antioxidant (Ohnishi *et al*., 2004), antidiabetic (Latifi *et al*., 2019) and anticancer (Kim *et al*., 2013) agent. As this bioflavonoid possess only one -OH group in its chemical structure, we used this drug molecule for our research to overcome the confusion of drug attachment site. The formulated nanoparticle will surely attach at the single -OH group present. As metal, we choose copper (Khalid *et al*., 2015), zinc (Ghanta *et al*., 2013) and cadmium (Salam *et al*., 2018) as because they all can be synthesized by reduction method with borohydrate. So the computer generated model structure could be done with the metal and boron atoms only. From this study we can have a better idea about the formation and developed of metal nanocomposite structures.

METHODS

During the synthesis of nanoparticles and their composites, one drug molecule may interact with more than one metal atom. We know that Bioflavonoids are polyphenolic in nature which contains many -OH groups in its chemical structure. To avoid the confusion that which free -OH group will take part in the interaction with metal nanoparticle, we selected ferulic acid (figure 1) which has only one free -OH group in its molecular structure. Metals we selected for our study were Copper (Cu), Zinc (Zn), Cadmium (Cd), as these metals have been reported for having capability to synthesize nanoparticles by many research groups. Not only that, all these three metals can formulate nanoparticles by the reduction method with borohydrate compound (Ghanta *et al*., 2013; Khalid *et al*., 2015; Salam *et al*., 2018). Here, we used Avogadro software for windows (Hanwell *et al*., 2012) to compose the structure of nanoparticles and their conjugates with ferulic acid. At very beginning we constructed the chemical structure of ferulic acid and allowed it for energy minimization. The structure showed the level of energy as we also found in our previous study (Hazra and Pal, 2020a).

After we noticed that the borohydrate is the common reducing agent for all 3 metal nanoparticles, we constructed the nanoparticle model structures in such a way that metal atoms and boron atom took part in formation of the particles. First we attached three metal atoms together with themselves and boron was attached to each metal atoms as first hypothetical model structure. In our second hypothetical model structure, we bonded three metal atoms through three boron atoms.

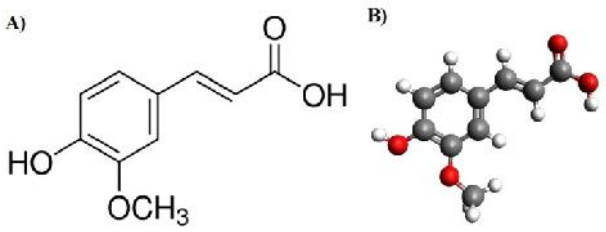

Figure 1. A) Chemical structure of ferulic acid and B) Model structure of ferulic acid derived in Avogadro software (Hazra and Pal, 2020a)

Both model structures were constructed for all three metals (Zn, Cd and Cu) under consideration of our present study. Every structure was then subjected for energy minimization. From this experiment, it was observed that the structures constructed through second hypothesis exhibited much less energy than that of first hypothesis. Hence, we selected the second hypothetical model structures for further study. After that we took six metal atoms (Zn, Cd and Cu) and four boron atoms for the formation of nanoparticle model structures according to our second hypothesis. All structures were subjected for energy minimization. After the formation of nanoparticle model structure with six metal atoms, we went one step higher i.e. again we constructed model structures of nanoparticles with nine metal atoms. In these structures also we incorporated boron atoms in between the metal atoms. So, for nine metal atoms to be connected through boron, we required six boron atoms. The energy minimizations of all model structures were performed and the energy levels were listed.

At last, we tagged ferulic acid with all three metal nanoparticles (consisting of nine metal atoms and six boron atoms) to formulate the ferulic acid nanoparticle composite model structure. The bonding between the molecules is done through the boron atom of the nanoparticle and oxygen atom of single -OH group of ferulic acid.

RESULTS AND DISCUSSION

According to the first hypothesis described in methodology section, at first we plotted three atoms of each metal (Zn, Cd and Cu) and make single bonds among the atoms. Then three Boron atoms were bonded with the metal atoms at three corners of the structure and energy minimization was done for each structure. We gave the structures name as Zn_1, Cd_1 and Cu_1. The structures are depicted in figure 2 (figure 2A, figure 2B and figure 2C). The energy levels of all these structures are also listed in table 1.

Table 1. List of energy possessed by nanoparticle model structures with three metal atoms and three Boron atoms using two different hypotheses

Metal	Compound	Energy (KJ / mol)
Zinc (Zn)	Zn_1	194.397
	Zn_2	5.015
Cadmium (Cd)	Cd_1	128.354
	Cd_2	4.863
Copper (Cu)	Cu_1	207.953
	Cu_2	6.701

As per our second hypothesis, we plotted three metal atoms and in between each atom, Boron atom was plotted. All metal atoms were bonded through Boron atoms, not directly to each

other. For three different metals, this type of structures have been formulated and subjected for energy minimization. We named these structures as Zn_2, Cd_2 and Cu_2. The energy levels of these structures have also been listed in table 1 and the model structures are shown in figure 2 (figure 2C, figure 2D and figure 2E).

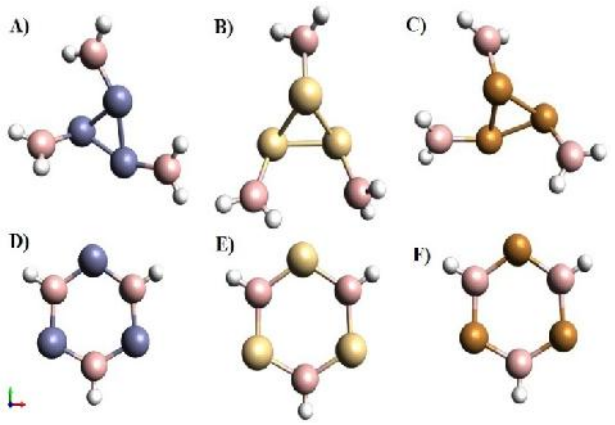

Figure 2. Model structure of A) Zn_1, B) Cd_1, C) Cu_1, D) Zn_2, E) Cd_2 and F) Cu_2

By comparing the structures obtained from both the hypothesis, it was observed that all structures composed by second hypothesis exhibited much lower energy that of the first hypothesis. Hence we consider the second hypothetical structures to be more stable and energetically favourable. Then we tried to attach more metal atoms in the next level of structure formation.

Here we took six metal atoms for Zn, Cd and Cu separately and four Boron atoms in between the metals. These structures are then stabilized with their minimum energy levels. Their structures were named as Zn_3, Cd_3 and Cu_3 respectively and depicted in figure 3 (figure 3A, figure 3B and figure 3C). The energy levels were listed in table 2.

Table 2. List of energy levels of nanoparticle model structures with six metal and four Boron atoms as well as nine metal and six Boron atoms

Metal	Compound	Energy (KJ / mol)
Zinc (Zn)	Zn_3	27.246
	Zn_4	60.367
Cadmium (Cd)	Cd_3	30.95
	Cd_4	63.428
Copper (Cu)	Cu_3	43.82
	Cu_4	67.297

After successfully constructing the nanoparticle model structures with six metal and four Boron atoms, we jumped into one step higher where we plotted nine metal and six Boron atoms bonded together to form representative nanoparticle structure.

As our second hypothesis worked better, we integrated the Boron atoms in between the metal atoms and likewise we made nanoparticle model structures for all three metals i.e. for Zn, Cd and Cu. These structures were given names as Zn_4 (figure 3D), Cd_4 (figure 3E) and Cu_4 (figure 3F) respectively and allowed to undergo for energy minimization. The energy levels of these model structures are listed in table 2.

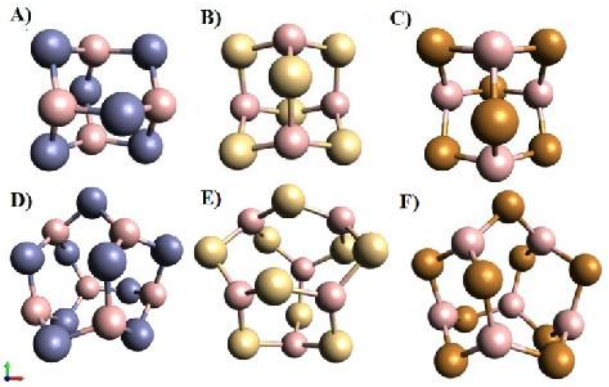

Figure 3. Model structure of A) Zn_3, B) Cd_3, C) Cu_3, D) Zn_4, E) Cd_4 and F) Cu_4.

After formulation of model nanostructures, we tried to observe the interaction pattern between the nanoparticles and a drug molecule. As stated in the introduction section, we selected ferulic acid for this study because it contains only one -OH group in its chemical structure. The single -OH group strongly determines where the nanoparticles could be bound with the drug molecule. In the nanoparticle, the Boron atom was interacted with -OH group of the ferulic acid. Similarly we constructed three ferulic acid – metal nanocomposite model structures with three different metals (Zn, Cd and Cu) and energy minimizations were performed. These formulated nanocomposite model structures were named as Zn_FA_1 (figure 4A), Cd_FA_1 (figure 4B) and Cu_FA_1 (figure 4C).

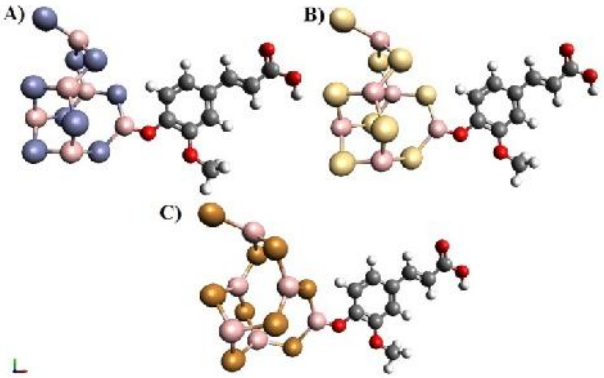

Figure 4. Model structure of A) Zn_FA_1, B) Cd_FA_1 and C) Cu_FA_1

To characterize the structures, we also calculated the bond lengths between the Boron atoms of nanoparticle and the Oxygen atom of drug molecule as well as the Oxygen and Carbon atoms of ferulic acid as these two bonds are making the bond angle at the interaction. Along with the bond lengths, the bond angles between Boron–Oxygen–Carbon atoms (B-O-C bond angle) for all three nanocomposites were measured through the same software. The values on bond lengths and angles are listed in table 3. Many research groups have studied on ferulic acid or any other flavonoid and nanoparticle composite structures with several metals like Zn (Babu *et al*., 2017), Fe (Angkawijaya *et al*., 2011), Cu (Lopez *et al*., 2019) etc, but study on their mode of interaction have not been revealed yet in detail. Our lab is engaged in this kind of studies for past few years where we found that not all but few metals are energetically favourable for making nanocomposite structures with several drug molecules (Hazra *et al*, 2020; Hazra and Pal, 2020b; Hazra and Pal, 200c).

Table 3. List of energy levels of all three nanocomposite structures (Zn_FA_1, Cd_FA_1 and Cu_FA_1) along with their bond angles and bond lengths

Metal	Compound	Energy (KJ / mol)	B – O – C Bond Angle (degree)	Bond Length (Å)	
				B - O	O - C
Zinc (Zn)	Zn_FA_1	161.402	128.8	1.450	1.361
Cadmium (Cd)	Cd_FA_1	160.8	128.6	1.450	1.361
Copper (Cu)	Cu_FA_1	173.08	128.9	1.451	1.361

It is very much important to find the most probable structure before performing experiments in wet laboratory condition so that researcher's can have a preliminary idea about the nanocomposite structures and its properties prior to synthesizing them *in vitro*.

Conclusion

From our present study, we can conclude that if the Boron atoms get incorporated in between the metal atoms, the formulated nanoparticle structures may possess less energy than the Boron atoms when attached to the corner allowing the metals to be interacted amongst them directly. Accordingly we constructed our nanoparticles with six and nine metal atoms (Zn, Cd and Cu). When the nanoparticles are in free form, Zn showed minimum energy level which is 60.367 KJ / mol with respect to others. Interestingly when ferulic acid was attached to the nanoparticles, Cadmium nanoparticle exhibited lowest energy level in Cadmium ferulic acid nanocomposite model structure (160.8 KJ / mol), although Zn showed almost similar but little higher energy which is 161.402 KJ / mol. Hence both Zn and Cd may be used for nanocomposite formation with ferulic acid. Copper may also be used but its higher energy level suggests energetically less favourable for formulating this kind of nanocomposite structure with ferulic acid which makes Copper less suitable for this purpose than Zinc and Cadmium.

REFERENCES

Adams C. P., Walker K. A., Obare S. O. and Docherty K. M., 2014. "Size-Dependent Antimicrobial Effects of Novel Palladium Nanoparticles", PlosOne, 9(1): e85981.

Angkawijaya A. E., Fazary A. E., Hernowo E., Taha M. and Ju Y. H., 2011. "Iron (III), Chromium (III), and Copper (II) Complexes of LNorvaline and Ferulic Acid", Journal of Chemical & Engineering Data, 56(3): 532–540.

Babu E. P., Subastri A., Suyavaran A., Premkumar K., Sujatha V., Aristatile B., Alshammari G. M., Dharuman V. and Thirunavukkarasu C., 2017. "Size Dependent Uptake and Hemolytic Effect of Zinc Oxide Nanoparticles on Erythrocytes and Biomedical Potential of ZnO-Ferulic acid Conjugates", Scientific Reports, 7: 4203.

Duncan B., Kim C. and Rotello V. M., 2010. "Gold nanoparticle platforms as drug and biomacromolecule delivery systems", Journal of Controlled Release, 148(1): 122–127.

Ghanta S. R., Rao M. H. and Muralidharan K., 2013. "Single-pot synthesis of zinc nanoparticles, borane (BH3) and closo-dodecaborate (B12H12) 2− using LiBH4 under mild conditions", Dalton Transactions, 42: 8420–8425.

Guo D., Wu C., Li J., Guo A., Li Q., Jiang H., Chen B. and Wang X., 2009. "Synergistic Effect of Functionalized Nickel Nanoparticles and Quercetin on Inhibition of the SMMC-7721 Cells Proliferation", Nanoscale Research Letters, 4: 1395–1402.

Hanwell M. D, Curtis D. E., Lonie D. C., Vandermeersch T., Zurek E. and Hutchison G. R., 2012. "Avogadro: an advanced semantic chemical editor, visualization, and analysis platform" Journal of Cheminformatics, 4: 17.

Hazra D. and Pal R., 2020a, "Nanocomposite Formulation of Ferulic Acid with Different Metals Using Computational Method", Advanced Nano Research, 3 (1): 40 – 45.

Hazra D. and Pal R., 2020b. "Speculation of metal for suitable Lutionin – Metal nanocomposite formulation through *in silico* approach", International Journal of Advanced Research, 8 (6): 219 – 224.

Hazra D. and Pal R., 2020c. Representative model structure formulation of gold nanocomposite *in silico* with three different flavonoids", Life Science Archives, 6(5): 1953 – 1962.

Hazra D., Chatterjee D. and Pal R., 2020. "Designing of nanocomposite model structure using Gallic acid and Ellagic acid with four different metals" International Journal of Life Sciences, 8(3): 556 – 562.

Khalid H., Shamaila S., Zafar N., 2015. "Synthesis of copper nanoparticles by chemical reduction method", Science International Lahore, 27(4): 3085-3088.

Kim H. J., Ryu K., Kang J. H., Choi A. J., Kim T. and Oh J. M., 2013. "Anticancer Activity of Ferulic Acid-Inorganic Nanohybrids Synthesized via Two Different Hybridization Routes, Reconstruction and Exfoliation-Reassembly", The Scientific World Journal, 2013: 421967.

Kim J., Shirasawa T. and Miyamoto Y., 2010. "The effect of TAT conjugated platinum nanoparticles on lifespan in a nematode Caenorhabditis elegans model", Biomaterials, 31(22): 5849–5854.

Kruk T., Szczepanowicz K., Stefanska J., Socha R. P. and Warszynski P., 2015. "Synthesis and antimicrobial activity of monodisperse copper nanoparticles", Colloids and Surfaces B: Biointerfaces, 128 (1): 17 – 22.

Latifi E., Mohammadpour A. A., Fathi B. H. and Nourani H., 2019. "Antidiabetic and antihyperlipidemic effects of ethanolic Ferula assafoetida oleo-gum-resin extract in streptozotocin-induced diabetic wistar rats", Biomedicine & Pharmacotherapy, 110: 197- 202.

Lopez P. G., Lazaro N., Alvarado-Beltrán C. G., Pineda A., Balu A. M. and Luque R., 2019. "One-Pot Cu/TiO2 Nanoparticles Synthesis for Trans-Ferulic Acid Conversion into Vanillin", Molecules, 24(21): 3985.

Mahdy S. A., Raheed Q. J. and Kalaichelvan P. T., 2012. "Antimicrobial Activity of zero-valent Iron Nanoparticles", International Journal of Modern Engineering Research", 2(1): 578–581.

Ohnishi M., Matuo T., Tsuno T., Hosoda A., Nomura E., Taniguchi H., Sasaki H. and Morishita H., 2004. "Antioxidant Activity and Hypoglycemic Effect of Ferulic Acid in STZ-induced Diabetic Mice and KK-Ay Mice", Biofactors, 21(1-4): 315-319.

Qi L., Colfen H. and Antonietti M., 2001. "Synthesis and Characterization of CdS Nanoparticles Stabilized by Double-Hydrophilic Block Copolymers", Nano Letters, 1(2): 61–65.

Riaz S., Rana N. F., Hussain I., Tanweer T., Nawaz A., Menaa F., Janjua H. A., Alam T., Batool A., Naeem A., Hameed M. and Ali S. M., 2020. "Effect of Flavonoid-Coated Gold Nanoparticles on Bacterial Colonization in Mice Organs" Nanomaterials, 10(9): 1769.

Rojas S., Carmona F. J., Maldonado C. R., Horcajada P., Hidalgo T., Serre C., Navarro J. A. R. and Barea E., 2016. "Nanoscaled Zinc Pyrazolate Metal–Organic Frameworks as Drug-Delivery Systems", Inorganic Chemistry, 55 (5): 2650–2663.

Salam W. T., Ikram M., Shahzadi I. , Imran M., Junaid M., Aqeel M., Anjum S. , Shahzadi A., Afzal H., Sattar U., Asghar A., Wahab A., Naz M., Nafees M. and Ali S., 2018. "Doping Dependent Structural, Optical, Thermal and Catalysis Properties of Synthesized Cadmium Sulfide Nanoparticles", Nanoscience and Nanotechnology Letters, 10: 1–9.

Santos C. A. D., Seckler M. M., Ingle A. P., Gupta I., Galdiero S., Galdiero M., Gade A. and Rai M., 2014. "Silver Nanoparticles: Therapeutical Uses, Toxicity, and Safety Issues", Journal of Pharmaceutical Sciences, 103(7): 1931–1944.

Shafey A. M. E., 2020. "Green synthesis of metal and metal oxide nanoparticles from plant leaf extracts and their applications: A review" Green Processing and Synthesis, 9(1): 304 – 339.

Shi C., Zhang X., Sun Y., Yang M., Song K., Zheng Z., Chen Y., Liu X., Jia Z., Dong R., Cui L. and Xia X., 2016. "Antimicrobial Activity of Ferulic Acid Against *Cronobacter Sakazakii* and Possible Mechanism of Action", Food borne Pathogens and Disease, 13(4): 196-204.

Twi-global, 2021. "Technical knowledge of Nanoparticle "https://www.twi-global.com/technical-knowledge/faqs/what-are-nanoparticles

Viau G., Brayner R., Poul L. , Chakroune N. , Lacaze E., Vincent F. F. and Fievet F., 2003, "Ruthenium Nanoparticles: Size, Shape, and Self Assemblies", Chemistry of Materials, 15(2): 486 – 494.

Xu L., Liu D., Chen D., Liu H. and Yang J., 2019. "Size and shape controlled synthesis of rhodium nanoparticles", Heliyon, 5(1): e01165.

Yin W., Chai W., Wang K., Ye W., Rui Y. and Tang B., 2019. "Facile synthesis of Sb nanoparticles anchored on reduced graphene oxides as excellent anode materials for lithium-ion batteries", Journal of Alloys and Compounds, 797: 1249–1257.

Zhu H., Liang Q. H., Xiong X. G., Chen J., Wu D., Wang Y., Yang B., Zhang Y., Zhang Y. and Huang X., 2014. "Anti-Inflammatory Effects of the Bioactive Compound Ferulic Acid Contained in Oldenlandia diffusa on Collagen-Induced Arthritis in Rats", Evidence-Based Complementary and Alternative Medicine, 2014: 573801.

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