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A molecular modeling investigation using DFT studies to examine the interaction between a melanin pigment and a Buckwheat

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A B S T R A C T

This study presents a summary of the use of buckwheat with its melanin pigment composition in human skin. The internal energy of buckwheat, as determined by the density functional function of molecular studies using the Goussian 09 and Hyperchem 08 programs, exhibited a value that was found to be nearly identical to that of melanin, which was found to be (-1109 Hartree, -1101 Hartree), respectively. To corroborate these findings, the molar number of buckwheat was incorporated in a ratio of 1:2, resulting in a notable reduction in polar moment by 1.759730 Debye. This was accompanied by an increase in stability and a decrease in polar moment, which in turn led to a reduction in activity and a limitation of the effect of UV radiation on melanin pigment.

1 Introduction

Buckwheat (Fagopyrum esculentum) is a member of the Polygonaceae family and constitutes a dietary staple in arid and semi-arid regions across the globe. Buckwheat is a species that is found in a multitude of locations across the globe. However, it is predominantly cultivated in mountainous regions of Russia and China.[1-4] In 2019, global buckwheat production reached 3.5 million tons, with Russia accounting for the majority of this output at 1.5 million tons. China, in contrast, is the second-largest producer, with an estimated 0.9 million tons.[5] The most widely cultivated species of buckwheat are common buckwheat (CB; Fagopyrum esculentum) and tartary buckwheat (TB; Fagopyrum tataricum). The grains of common buckwheat and tartary buckwheat are frequently milled or groats in order to obtain flour, which is then used as an ingredient in a variety of processed foods, including buckwheat tea, flour, bread, muffins, noodles, and other food products.[4, 6, 7] Buckwheat has garnered increasing attention from the scientific community due to its purported pharmaceutical and health benefits. These include anticancer, anti-tumour, anti-inflammatory, hepatoprotective, anti-hypertension, anti-diabetic, neuroprotective, cholesterol-lowering and cognition-improving properties, as evidenced by numerous studies. The aforementioned health benefits are attributed to the chemical compounds present in buckwheat, including proteins, balanced amino acids, dietary fibre, carbohydrates, fatty acids, vitamins and minerals. These compounds possess beneficial properties with regard to the treatment of chronic diseases.[8-11] Furthermore, buckwheat is hypothesised to possess elevated concentrations of functional compounds with antioxidant properties. These compounds comprise a substantial number of chemical compounds, including flavonoids and polyphenols. Buckwheat is a rich source of flavonoids, including rutin, quercetin, quercitrin,

isovitexin, vitexin, orientin and homoorientin. The chemical structures of the buckwheat flavonoids are illustrated in Figure 1 and provided in Table1.[12-14]

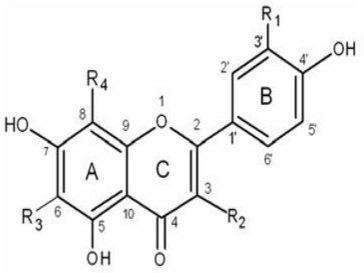

Figure 1. Chemical structure of buckwheat flavonoids. [12]

Table 1. Chemical structure of Buckwheat flavonoids.[12]

Buckwheat Flavonoids	R_1	R_2	R_3	R_4
rutin	OH	rutinose	H	H
quercetin	OH	OH	H	H
quercitrin	OH	rhamnose	H	H
orientin	OH	H	H	glucose
homoorientin	OH	H	glucose	H
vitexin	H	H	H	glucose
isovitexin	H	H	glucose	H

Melanin is a phenolic pigment polymer that originates from the amino acid tyrosine. Melanin is present in varying degrees of pigmentation in human skin and is responsible for the colour of the skin, hair and eyes. Its presence is determined mainly by the ability of specialized cells to synthesise insoluble, brown-black eumelanin and the alkaline-soluble, yellow-reddish pheomelanin.[15, 16] The brown-black eumelanin from different sources: animal melanin, plant melanin, fungal melanin, synthetic melanin and bacterial melanin is heterogeneous macromolecule derived by the oxidation and polymerization of phenolic compounds to intermediate phenols and their resulting quinones. Melanin defined with the molecular formula $C_{18}H_{10}O_4N_2$,anaverage mass of 318.3 for the minimal unit, and the systematic name 3,8-dimethyl-2,7-dihydrobenzo[1,7]isoindolo[6,5,4 cd]indole-4,5,9,10-tetrone, and its depicted at Figure 2.[17-19] Melanin has the ability to absorb harmful UV (ultraviolet) rays. Ultraviolet B (UVB), Ultraviolet A (UVA), and blue visible light are all protected from damage by melanin, which also protects skin cells from reactive oxygen species (ROS) generated during UV-induced oxidative stress on the skin.[20]

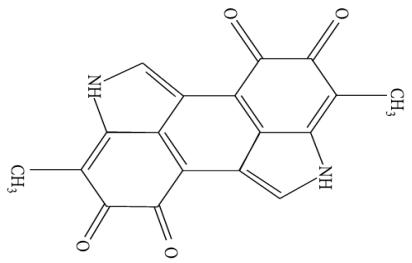

Figure 2. Chemical structure of melanin pigment.

The aim of the present study is to provide a contemporary evaluation of the diverse beneficial components present in buckwheat. The hypothesis that the dark colours in seeds are due to the presence of melanin has been tested for the aforementioned species using chemical assays that are related to the previously mentioned spectroscopic methods.[21-23] The accompanying species have been identified as containing melanin, including watermelon, sunflower, buckwheat, grape, tomato, fragrant olive, night jasmine, sesame, ipomoea, black mustard, rape, chestnut, garlic, oat, and barley, among others.[19, 23-33] Moreover, the presence of melanin in intact seed tissues has been corroborated through the utilisation of diagnostic physicochemical tests. Additionally, research has demonstrated that flavonoids, specifically rutin and quercetin, are distributed throughout buckwheat plants, occurring in the leaves, grain, and flowers.[34] The potential for medical application of quercetin and rutin is based on their antioxidant properties.[35] The sun emits energy in a wide range of electromagnetic radiation, classified into different spectral regions (Figure 3A). These include ultraviolet radiation (UVR), which has wavelengths between 180 and 380 nm, visible light (VL), which has wavelengths of approximately 380 to 800 nm, and infrared light (range 1–3 µm). The damaging effect on the skin is largely dependent on the wavelength of the radiation in question. In general, shorter wavelengths possess greater energy, potential, and harmfulness to the skin. Ultraviolet radiation (UVR) is divided into several subdivisions within the ultraviolet spectrum. In the field of photodermatology, the most commonly used subdivisions are UVC (180–280 nm), UVB (280–320 nm), and UVA (320–380 nm). The ultraviolet B (UVB) radiation is more cytotoxic than the ultraviolet A (UVA) radiation. The most energetic UVB rays display low penetrance and are responsible for the majority of carcinogenic effects of sunlight. They cause direct cellular biochromes (mainly cutaneous pigments, proteins or DNA and nucleic acid) damage at the basal epidermis layer by absorbing energy within this range. UVA and visible light have the greatest penetrating power, enabling them to reach the dermis layer of the skin and induce tanning. UVA causes indirect damage, primarily through the generation of reactive oxygen species (ROS). It is fortunate that high-energy UVC rays

are unable to reach the Earth's surface and are effectively attenuated by the ozone layer.[36, 37]

The ultraviolet (UV) light has two distinct mechanisms by which it damages the DNA. The initial consequence is the formation of cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidone photoproducts (6-4PPs), which entail covalent bonding between adjacent pyrimidine bases (cytosine and thymine) within the DNA strand. This results in distortion of the DNA structure, which in turn impedes the replication process and may potentially give rise to mutations. The second mechanism is indirect. During ultraviolet radiation exposure, there is an increase in the production of reactive oxygen species (ROS), including superoxide anion, hydrogen peroxide, and singlet oxygen. These species have the potential to break down DNA and cause erythema in mammals (Figure 3B). In both instances, the cumulative damage to DNA may ultimately result in the development of cancer.[36, 37]

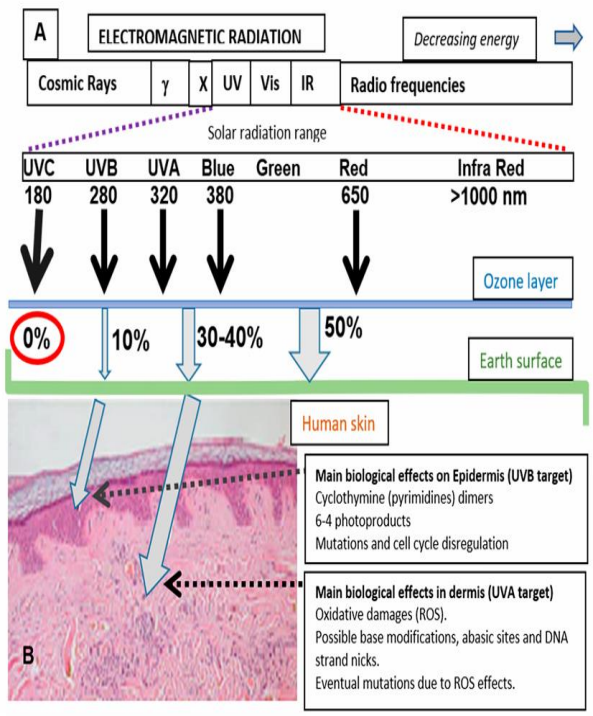

Figure 3. Solar radiation reaching Earth's surface, skin penetrance, and biological effects. (A) Approximate percentage (%) of the total solar radiation reaching Earth's surface for different wavelength regions. (B) Skin penetrance of UVB and UVA.[36]

Long-term exposure to ultraviolet radiation represents a significant risk factor for the development of various dermatological conditions, including irreversible skin photoaging, sunburn, redness, pain, solar keratosis, and loss of transparency. Additionally, it has been linked to the onset of photodermatoses, skin cancer, thermal discomfort, and premature skin aging.[38, 39]However, the development of skin cancer is a multifactorial process, with a number of potential causes including exposure to chemicals, the human papillomavirus or a weakened immune system. Nevertheless, ultraviolet radiation represents the most significant risk factor for the development of skin cancer.[40]

In recent times, researchers engaged in the field of skin protection have demonstrated a notable inclination towards the utilisation of natural products as a means of safeguarding the skin from UV phototoxic damage. These natural products, substances or plant extracts or isolated plant compounds with aromatic rings in their structures, such as flavonoids or polyphenols, have been demonstrated to possess a significant capacity for absorbing both UVA and UVB rays.[41] Furthermore, they frequently demonstrate robust antioxidant characteristics by neutralising detrimental free radicals within the body. Given these properties, it seems reasonable to suggest that natural products will become a significant part of the future of cosmetics.[42-44] The market for natural cosmetic products is one of the fastest growing sectors in the global economy.[45]
Consequently, the majority of research into natural UV filters is concentrated on the UVB range, given that all flavonoid components possess aromatic rings (conjugated bonds) and chemical groups typically exhibit a more extensive absorption spectrum, encompassing a wavelength range of 200–400 nm. This renders them well-suited for utilisation as sunscreen agents.[46] The term "photoprotection" is defined as a biological mechanism that enables organisms to mitigate the effects of solar radiation at the cellular level, thereby reducing their exposure to ultraviolet radiation (UVR).[47] It represents a primary strategy for the prevention of UVR-related dermatological conditions. Furthermore, it has been demonstrated that natural products can enhance dermal conditions by stimulating the DNA repair mechanisms of damaged skin cells.[48] It can be reasonably deduced that natural substances derived from plants possess distinctive advantages in the development of sunscreen filters when compared to synthetic sunscreen filters, which are inherently challenging to synthesis, exhibit poor photostability and high sensitisation.[37]
Moreover, melanin pigments can be employed in a variety of applications due to their physico-chemical characteristics. These include the protection of UV-Vis spectra, electrochemical processes, and medical applications aimed at elucidating the aetiology of melanin-related diseases.[49]

Nevertheless, previous research has indicated that the natural products in question are unable to assist melanin pigment in resisting the effects of ultraviolet radiation

and the subsequent oxidation process. Moreover, previous studies have not determined the polarity and energy that elucidate the pigment's stability during exposure to radiation. In this context, a deeper comprehension of the interaction between a melanin pigment and a buckwheat-based product, derived from optimised structures, is essential. Additionally, comparisons with other natural products have not been conducted. In view of the aforementioned findings, this study employed buckwheat as a means of assessing its potential for enhancing and safeguarding melanin pigmentation. The objective was to identify the most stable molecular model.

Problem statement & Objectives

Prior research has demonstrated that the natural products in question lack the capacity to assist melanin pigment in resisting the effects of ultraviolet radiation and the subsequent oxidation process. Furthermore, previous studies have not determined the polarity and energy that elucidate the pigment's stability during exposure to radiation. Furthermore, no comparisons have been made with other natural products. In light of the aforementioned findings, this study employed buckwheat as a means of assessing its potential for enhancing and safeguarding melanin pigmentation. The objective was to identify the most stable molecular model.

2 Computational Methods

After years of developing increasingly precise and computationally expensive semi-empirical models, John came to the realisation that improvements to the algorithms could render non-experimental calculations (then referred to as 'ab initio') sufficiently rapid to be applied to large problems. This type of theory constituted the focus of his work for the final three decades of his career. His paper on the STO-3G basis set is still one of his most frequently cited. [50]

Following the development of a new algorithm in collaboration with his colleague Warren Hehier, which markedly enhanced the processing speed of Haretre Voc accounts, the subsequent program, Gaussian 70, was made available through QCPE.[51]The findings of previous research conducted by other researchers, such as Polyatom, have been presented to numerous academic research groups and their applications. Nevertheless, due to its high processing speed and user-friendliness, Gaussian 70 has become the most widely used ab initio program among researchers today. The G09 version employed in this study was developed on the basis of Gaussian 70. During the 1970s, John and his team developed more sophisticated ab initio strategies, including the use of larger basis sets (6-31G, 6-31G*, etc.) and the incorporation of electron correlation beyond Hartree-Fock. Furthermore, they conducted a comparative analysis of several competing methodologies, including configuration interaction, perturbation theory, and coupled cluster.[52]

3 Results & Discussion

The optimized structures of melanin pigment and the buckwheat are shown in Figure 4. The calculation of the total internal energy, polar moment, and wavelength of ultraviolet absorption for the melanin pigment and the buckwheat will be presented. Subsequently, the buckwheat compounds will be added individually to the melanin pigment in order to observe the differences in internal energy, polar moment, and wavelength of ultraviolet absorption. It can be expected that the lowest energy will be the most stable, and the polar moment the most stable and more flexible. These details are presented in Table 2 and Figures 4(a) and 4(b) for reference.

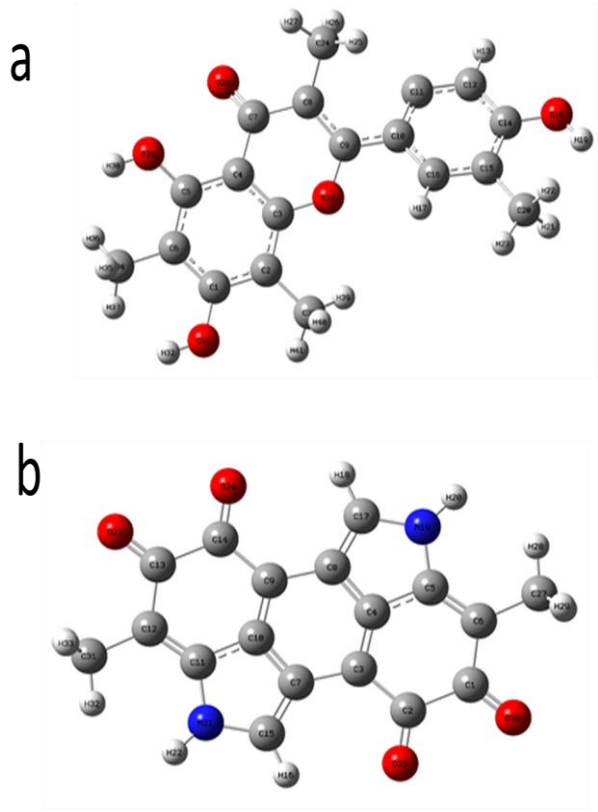

Figure 4: Optimized geometry of the (a) buckwheat, (b) melanin pigment

Table 2.The data presented included the binding energy, dipole moment and ultraviolet absorbance values between melanin and buckwheat.

Chemical Compound	Energy-DFTcalculation (hartree)	Dipole moment, Debye	λ_{max} (nm)
Melanin	-1101.917153	0.111511	1171.17
Buckwheat	-1109.880243	6.047186	701.42
M-B (1:1)	-2212.546858	5.006774	1258.99
M-B (1:2)	-3323.2000792	1.759730	1197.15
M-B (1:3)	-4383.200520	23.836434	647.26

Table 2 presents the inhibitory force of the physically interfering compounds between melanin pigment and varying proportions of buckwheat. Upon alteration of the proportions and subsequent increase in the quantity of buckwheat, a reduction in internal energy is observed, accompanied by enhanced stability. This is predicated on the assumption that a reduction in internal energy is indicative of greater accuracy and stability in chemical compounds. However, it was observed that the remaining physical values, namely the polar moment and absorbance, did not exhibit a dependence on the increase in the proportion of buckwheat. Furthermore, the 1:2 ratio of buckwheat pigment and melanin exhibits the optimal energy and the best flexibility due to the decrease in the value of the polar moment among all the proportions shown. This gives it the characteristic of low polarity, i.e. a small number of side charges, which results in higher stability among the remaining proportions. Consequently, it shows greater inhibition. With regard to the increase in absorbance values, it should be noted that the theoretical calculations differ somewhat from the results obtained for the compounds in practice. However, it is important to emphasise that the measurement is the same. This implies that any compounds differ in absorbance value in practice, with the result for one compound being higher or lower than that for the second compound. Consequently, it can be observed that in the theoretical calculations, the same direction is indicated, whereby the first compound is either higher or lower than the second compound, with the same behaviour of the compounds in practice. However, it should be noted that the values will differ somewhat based on the readings of the computers used in the theoretical quantum mechanics calculations.

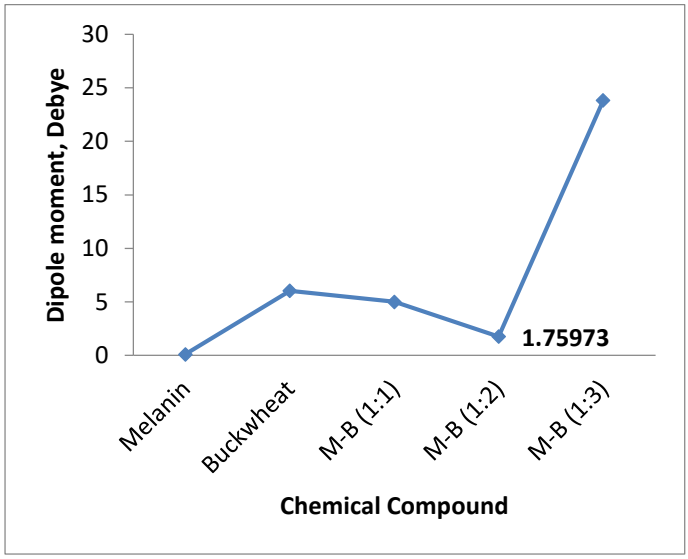

Figure 5. The polar moment values for melanin and buckwheat pigment compounds, presented individually and in combination.

Figure 5 demonstrates a reduction in the polar moment value of the melanin pigment complex when combined with the buckwheat compound. This decrease indicates an enhanced capacity to diminish melanin activity in response to UV radiation, as illustrated in Figure 7. This phenomenon occurs specifically at a ratio of 1:2, thereby affording the pigment a greater degree of protection.

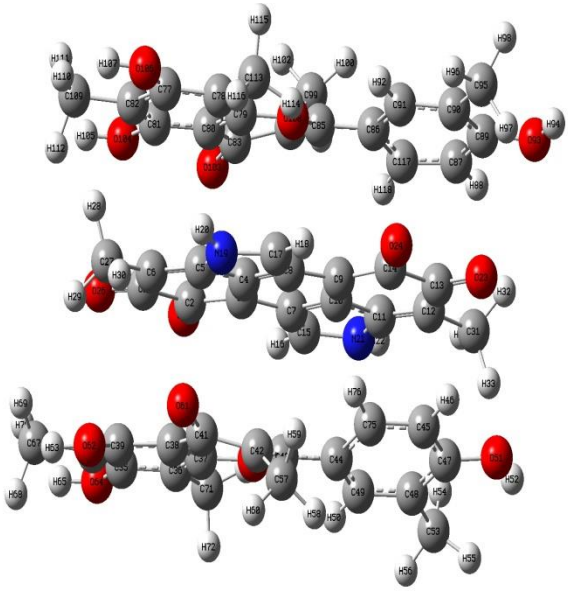

Figure 6. The inclusion complex is combined with melanin pigment and buckwheat in a ratio of 1:2.

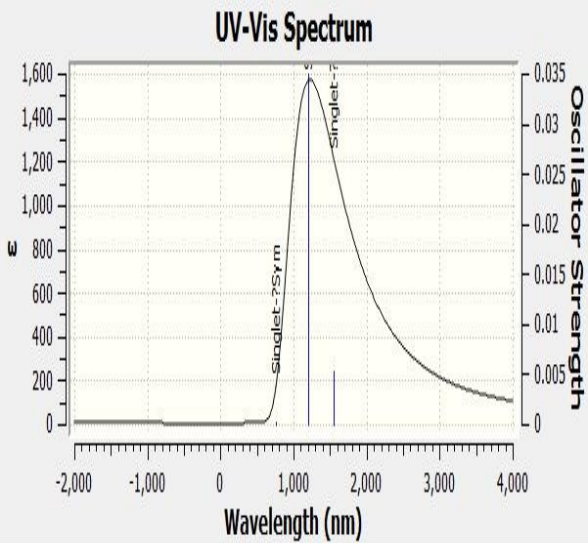

Figure 7. UV-vis curve of the inclusion complex formed between melanin and buckwheat in a 1:2 ratio is presented herewith.

4 Conclusions

The results demonstrate that the integration of the buckwheat compound with the melanin pigment compound at a ratio of 1:2 represents the optimal computational interference, resulting in the lowest energy, optimal internal stability, and the lowest polar moment. This, in turn, reduces the exchange of charges and increases the inhibition rate during exposure to ultraviolet rays at the optimal stable computational level. In addition, our work reveals the relationship between the structures of buckwheat with the melanin pigment, providing a basis for the future research towards the development of natural products cosmetics.

5 References

1. Yilmaz, H. Ö., Ayhan, N. Y., & Meriç, Ç. S. (2020). Buckwheat: A useful food and its effects on human health. Current Nutrition & Food Science, 16(1), 29-34.
2. Zou, L., Wu, D., Ren, G., Hu, Y., Peng, L., Zhao, J., ... & Xiao, J. (2023). Bioactive compounds, health benefits, and industrial applications of Tartary buckwheat (Fagopyrum tataricum). Critical reviews in food science and nutrition, 63(5), 657-673.
3. Begemann, J., et al., Facing tropane alkaloid contamination in millet–Analytical and processing aspects. 2021. **13**(2): p. 79-86.
4. Begemann, J., Ostovar, S., & Schwake-Anduschus, C. (2021). Facing tropane alkaloid contamination in millet–Analytical and processing aspects. Quality Assurance and Safety of Crops & Foods, 13(2), 79-86.
5. Pocienė, O., & Šlinkšienė, R. (2022). Studies on the possibilities of processing buckwheat husks and ash in the production of environmentally friendly fertilizers. Agriculture, 12(2), 193.
6. Diowksz, A., & Sadowska, A. (2021). Impact of sourdough and transglutaminase on gluten-free buckwheat bread quality. Food Bioscience, 43, 101309.
7. Yılmaz, H. Ö., & Meriç, Ç. S. (2024). Grains and Pulses in Diets of the Middle East and a Focus on Buckwheat. In Ancient and Traditional Foods, Plants, Herbs and Spices used in the Middle East (pp. 3-14). CRC Press.
8. Ruan, J., Zhou, Y., Yan, J., Zhou, M., Woo, S. H., Weng, W., ... & Zhang, K. (2022). Tartary buckwheat: An under-utilized edible and medicinal herb for food and nutritional security. Food Reviews International, 38(4), 440-454.
9. Verma, K. C., Rana, A. S., Joshi, N., & Bhatt, D. (2020). Review on common buckwheat (Fagopyrum esculentum Moench): A potent Himalayan crop. Ann. Phytomed, 9, 125-133.
10. Džafić, A., & Žuljević, S. O. (2022). The importance of buckwheat as a pseudocereal: Content and stability of its main bioactive components. Pseudocereals IntechOpen, 8, 79.
11. Luthar, Z., Golob, A., Germ, M., Vombergar, B., & Kreft, I. (2021). Tartary buckwheat in human nutrition. Plants, 10 (4), 700.
12. Zielińska, D., Turemko, M., Kwiatkowski, J., & Zieliński, H. (2012). Evaluation of flavonoid contents and antioxidant capacity of the aerial parts of common and tartary buckwheat plants. Molecules, 17(8), 9668-9682.
13. Raguindin, P. F., Itodo, O. A., Stoyanov, J., Dejanovic, G. M., Gamba, M., Asllanaj, E., ... & Kern, H. (2021). A systematic review of phytochemicals in oat and buckwheat. Food chemistry, 338, 127982.
14. Huda, M. N., Lu, S., Jahan, T., Ding, M., Jha, R., Zhang, K., ... & Zhou, M. (2021). Treasure from garden: Bioactive compounds of buckwheat. Food chemistry, 335, 127653.
15. Taylor, S. C. (2002). Skin of color: biology, structure, function, and implications for dermatologic disease. Journal of the American Academy of Dermatology, 46(2), S41-S62.
16. Del Bino, S., Ito, S., Sok, J., & Wakamatsu, K. (2022). 5, 6-Dihydroxyindole eumelanin content in human skin with varying degrees of constitutive pigmentation. Pigment Cell & Melanoma Research, 35(6), 622-626.
17. Solano, F. (2014). Melanins: skin pigments and much more—types, structural models, biological functions, and formation routes. New Journal of Science, 2014(1), 498276.
18. Meredith, P., & Sarna, T. (2006). The physical and chemical properties of eumelanin. Pigment cell research, 19(6), 572-594.
19. Nicolaus, R. A., Piattelli, M., & Fattorusso, E. (1964). The structure of melanins and

melanogenesis—IV: On some natural melanins. Tetrahedron, 20(5), 1163-1172.
20. Bhattacharya, B., Chauhan, D., Singh, A. K., & Chatterjee, M. (2021). Melanin based classification of skin types and their susceptibility to UV-induced cancer. Skin Cancer: Pathogenesis and Diagnosis, 41-67.
21. Dossou, S. S. K., Luo, Z., Wang, Z., Zhou, W., Zhou, R., Zhang, Y., ... & Wang, L. (2022). The dark pigment in the sesame (Sesamum indicum L.) seed coat: isolation, characterization, and its potential precursors. Frontiers in nutrition, 9, 858673.
22. BT, S. K., Hebbar, U. H., & Annapurna Singh, S. (2024). Isolation, purification, and physio-chemical characterization of melanin pigment from nigerseed hulls (Guizotia abyssinica). Preparative Biochemistry & Biotechnology, 1-9.
23. Kannan, P., & Ganjewala, D. (2009). Preliminary characterization of melanin isolated from fruits and seeds of Nyctanthes arbor-tristis. Journal of Scientific Research, 1(3), 655-661.
24. Gracheva, N. V., & Zheltobryukhov, V. F. (2016). A method for obtaining melanins from sunflower husk and studying its antioxidant activity. News Kazan Technol. Univ, 19, 154-157.
25. Glagoleva, A.Y., O.Y. Shoeva, and E.K.J.F.i.P.S. Khlestkina, Melanin pigment in plants: Current knowledge and future perspectives. 2020. **11**: p. 770.
26. Downie, A. B., Zhang, D., Dirk, L. M., Thacker, R. R., Pfeiffer, J. A., Drake, J. L., ... & Snyder, J. C. (2003). Communication between the maternal testa and the embryo and/or endosperm affect testa attributes in tomato. Plant Physiology, 133(1), 145-160.
27. Wang, H., Pan, Y., Tang, X., & Huang, Z. (2006). Isolation and characterization of melanin from Osmanthus fragrans' seeds. LWT-Food Science and Technology, 39(5), 496-502.
28. Lucia, P., Thomas, E., & Alessandra, N. (2012). Black Sesame Pigment: DPPH Assay-Guided Purification, Antioxidant/Antinitrosating Properties, and Identification of a Degradative Structural Marker.
29. Park, K. I. (2012). A bHLH protein partially controls proanthocyanidin and phytomelanin pigmentation in the seed coats of morning glory Ipomoea tricolor. Horticulture, Environment, and Biotechnology, 53, 304-309.
30. Yu, C. Y. (2013). Molecular mechanism of manipulating seed coat coloration in oilseed Brassica species. Journal of applied genetics, 54, 135-145.
31. Wang, L. F., & Rhim, J. W. (2019). Isolation and characterization of melanin from black garlic and sepia ink. Lwt, 99, 17-23.
32. Varga, M., Berkesi, O., Darula, Z., May, N. V., & Palágyi, A. (2016). Structural characterization of allomelanin from black oat. Phytochemistry, 130, 313-320.
33. Shoeva, O. Y., Mursalimov, S. R., Gracheva, N. V., Glagoleva, A. Y., Börner, A., & Khlestkina, E. K. (2020). Melanin formation in barley grain occurs within plastids of pericarp and husk cells. Scientific reports, 10(1), 179.
34. Kreft, I., Vollmannová, A., Lidiková, J., Musilová, J., Germ, M., Golob, A., ... & Luthar, Z. (2022). Molecular shield for protection of buckwheat plants from UV-B radiation. Molecules, 27(17), 5577.
35. Rosiak, N., Cielecka-Piontek, J., Skibiński, R., Lewandowska, K., Bednarski, W., & Zalewski, P. (2023). Do rutin and quercetin retain their structure and radical scavenging activity after exposure to radiation?. Molecules, 28(6), 2713.
36. Solano, F. (2020). Photoprotection and skin pigmentation: Melanin-related molecules and some other new agents obtained from natural sources. Molecules, 25(7), 1537.
37. Verma, A., Zanoletti, A., Kareem, K. Y., Adelodun, B., Kumar, P., Ajibade, F. O., ... & Dwivedi, A. (2024). Skin protection from solar ultraviolet radiation using natural compounds: a review. Environmental Chemistry Letters, 22(1), 273-295.
38. Merin, K. A., Shaji, M., & Kameswaran, R. (2022). A review on sun exposure and skin diseases. Indian Journal of Dermatology, 67(5), 625.
39. Svobodová, A., & Vostalova, J. (2010). Solar radiation induced skin damage: review of protective and preventive options. International journal of radiation biology, 86(12), 999-1030.
40. Cavinato, M., & Jansen-Dürr, P. (2017). Molecular mechanisms of UVB-induced senescence of dermal fibroblasts and its relevance for photoaging of the human skin. Experimental gerontology, 94, 78-82.
41. Działo, M., Mierziak, J., Korzun, U., Preisner, M., Szopa, J., & Kulma, A. (2016). The potential of plant phenolics in prevention and therapy of skin disorders. International journal of molecular sciences, 17(2), 160.
42. Burlando, B., Verotta, L., Cornara, L., & Bottini-Massa, E. (2010). Herbal principles in cosmetics: Properties and mechanisms of action. CrC Press.
43. Amberg, N., & Fogarassy, C. (2019). Green consumer behavior in the cosmetics market. Resources, 8(3), 137.
44. Desam, N. R., & Al-Rajab, A. J. (2021). The importance of natural products in cosmetics. Bioactive natural products for pharmaceutical applications, 643-685.
45. Sasounian, R., Martinez, R. M., Lopes, A. M., Giarolla, J., Rosado, C., Magalhães, W. V., ... & Baby, A. R. (2024). Innovative approaches to an eco-friendly cosmetic industry: a review of sustainable ingredients. Clean Technologies, 6(1), 176-198.
46. Mota, M. D., da Boa Morte, A. N., e Silva, L. C. R. C., & Chinalia, F. A. (2020). Sunscreen protection factor enhancement through supplementation with Rambutan (Nephelium lappaceum L) ethanolic extract. Journal of Photochemistry and Photobiology B: Biology, 205, 111837.
47. Lingwan, M., Pradhan, A. A., Kushwaha, A. K., Dar, M. A., Bhagavatula, L., & Datta, S. (2023). Photoprotective role of plant secondary metabolites: Biosynthesis, photoregulation, and prospects of metabolic engineering for enhanced protection under excessive light. Environmental and Experimental Botany, 209, 105300.

48. Kaur, P., Purewal, S. S., Sandhu, K. S., & Kaur, M. (2019). DNA damage protection: an excellent application of bioactive compounds. Bioresources and Bioprocessing, 6, 1-11.

49. Guo, L., Li, W., Gu, Z., Wang, L., Guo, L., Ma, S., ... & Chang, J. (2023). Recent advances and progress on melanin: from source to application. International journal of molecular sciences, 24(5), 4360.

50. Newton, M. D., Lathan, W. A., Hehre, W. J., & Pople, J. A. (1969). Self-Consistent Molecular-Orbital Methods. III. Comparison of Gaussian Expansion and PDDO Methods Using Minimal STO Basis Sets. The Journal of Chemical Physics, 51(9), 3927-3932.

51. Hehre, W. J., Stewart, R. F., & Pople, J. A. (1969). Self-consistent molecular-orbital methods. I. Use of Gaussian expansions of Slater-type atomic orbitals. The Journal of Chemical Physics, 51(6), 2657-2664.

52. Hariharan, P. C., & Pople, J. A. (1973). The influence of polarization functions on molecular orbital hydrogenation energies. Theoretica chimica acta, 28, 213-222.

Appendix

****
Gaussian 09: IA32W-G09RevD.01 24-Apr-2013
09-Jun-2021
****
%chk=D:\mb_complex2;1_uv.chk

 # td b3lyp/6-31g nosymm geom=connectivity

1/38=1,57=2/1;
2/12=2,15=1,17=6,18=5,40=1/2;
3/5=1,6=6,11=9,16=1,25=1,30=1,74=-5/1,2,8,3;
4//1;
5/5=2,38=5/2;
8/6=1,10=2/1;
9/42=1,70=2/14;
6/7=2,8=2,9=2,10=2/1;
99/5=1,9=1/99;

Title Card Required

Symmetry turned off by external request.
Stoichiometry C56H46N2O14
Framework group C1[X(C56H46N2O14)]
Deg. of freedom 348
Full point group C1 NOp 1

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.669100	-0.270800	2.264200
2	6	0	-1.207300	-0.177000	2.747800
3	6	0	-0.941700	0.594500	3.968800
4	6	0	-1.989000	1.189200	4.557000
5	6	0	-3.359200	1.095400	4.123300
6	6	0	-3.734300	0.396000	3.040800
7	6	0	0.346600	0.789600	4.650700
8	6	0	-1.931100	1.978900	5.672800
9	6	0	-0.629800	2.241100	6.304900
10	6	0	0.407500	1.592900	5.756900
11	6	0	1.764200	1.620600	6.242000
12	6	0	2.139500	2.336600	7.314800
13	6	0	1.101000	3.145700	7.984600
14	6	0	-0.348900	3.103700	7.459400
15	6	0	1.576300	0.306100	4.401800
16	1	0	1.828300	-0.334100	3.609200
17	6	0	-3.177100	2.375600	5.986300
18	1	0	-3.432600	2.997100	6.792300
19	7	0	-4.101600	1.829000	5.061900
20	1	0	-5.041200	2.169000	4.915400
21	7	0	2.484200	0.771300	5.386100
22	1	0	3.489400	0.768900	5.288800
23	8	0	1.384100	3.848800	8.954200
24	8	0	-1.228300	3.780300	7.989700
25	8	0	-0.300100	-0.699000	2.102500
26	8	0	-2.934700	-0.878400	1.227500
27	6	0	-5.198700	0.290700	2.659900
28	1	0	-5.445700	1.061900	1.932100
29	1	0	-5.402000	-0.688500	2.227300
30	1	0	-5.824500	0.417100	3.543800
31	6	0	3.570400	2.300900	7.819500
32	1	0	3.899300	3.307000	8.077600
33	1	0	3.627200	1.674300	8.708600
34	1	0	4.233700	1.898400	7.053500
35	6	0	-2.394000	-3.525800	3.193400
36	6	0	-1.633200	-2.970500	4.243000
37	6	0	-2.282000	-2.240200	5.258900
38	6	0	-3.682100	-2.089600	5.254300
39	6	0	-4.443200	-2.701400	4.232500
40	6	0	-3.792000	-3.336200	3.153300
41	6	0	-4.282800	-1.337500	6.370400
42	6	0	-3.436800	-0.994800	7.517600
43	6	0	-2.037600	-1.079200	7.360300
44	6	0	-1.111000	-0.562400	8.292500
45	6	0	-0.465000	1.067400	9.991400
46	1	0	-0.700000	1.919000	10.560300
47	6	0	0.820600	0.508500	10.066000
48	6	0	1.147200	-0.592600	9.249700
49	6	0	0.187900	-1.104700	8.358800
50	1	0	0.441300	-1.930000	7.760700
51	8	0	1.730500	1.082300	10.888800
52	1	0	2.624700	0.736200	10.941600
53	6	0	2.524200	-1.230900	9.302500
54	1	0	3.208500	-0.675000	8.662900
55	1	0	2.901600	-1.234100	10.325200
56	1	0	2.469300	-2.261100	8.950600
57	6	0	-4.077800	-0.923100	8.894100
58	1	0	-3.353600	-1.186500	9.664800
59	1	0	-4.453300	0.084700	9.071000
60	1	0	-4.908500	-1.627100	8.951400
61	8	0	-5.412800	-0.854000	6.301900
62	8	0	-5.796000	-2.769900	4.324400
63	1	0	-6.309300	-3.217100	3.646900
64	8	0	-1.780600	-4.280800	2.247100
65	1	0	-2.291900	-4.686700	1.542800

66	8	0	-1.540800	-1.692800	6.256700
67	6	0	-4.605200	-3.852100	1.970900
68	1	0	-4.976600	-4.851900	2.194600
69	1	0	-5.448200	-3.189500	1.776000
70	1	0	-3.996600	-3.886300	1.067600
71	6	0	-0.125400	-3.196200	4.303300
72	1	0	0.077500	-4.157800	4.774600
73	1	0	0.300600	-3.190200	3.300400
74	1	0	0.366000	-2.408500	4.872900
75	6	0	-1.409800	0.561100	9.086200
76	1	0	-2.300600	1.094700	8.936000
77	6	0	-3.655400	3.516700	1.613200
78	6	0	-2.743800	3.969000	2.589600
79	6	0	-1.378100	3.641300	2.471300
80	6	0	-0.920700	2.829100	1.415200
81	6	0	-1.847800	2.337100	0.467700
82	6	0	-3.210100	2.697200	0.551900
83	6	0	0.535800	2.613300	1.320900
84	6	0	1.413500	3.429400	2.162000
85	6	0	0.851100	4.035900	3.303100
86	6	0	1.624500	4.576900	4.353900
87	6	0	3.712500	4.729900	5.609700
88	1	0	4.701000	4.407100	5.760400
89	6	0	3.143100	5.677300	6.474400
90	6	0	1.792900	6.042900	6.311100
91	6	0	1.051700	5.509600	5.241900
92	1	0	0.063300	5.833600	5.097400
93	8	0	3.900600	6.189600	7.473100
94	1	0	3.527600	6.824600	8.089200
95	6	0	1.129200	7.006400	7.277400
96	1	0	0.062900	7.079900	7.063500
97	1	0	1.259100	6.649400	8.299100
98	1	0	1.583100	7.992400	7.177500
99	6	0	2.717400	3.934600	1.565100
100	1	0	3.004300	4.879400	2.026600
101	1	0	3.503500	3.195800	1.720700
102	1	0	2.592900	4.100900	0.494600
103	8	0	1.042400	1.752700	0.601400
104	8	0	-1.446600	1.528500	-0.546000
105	1	0	-2.081000	1.203100	-1.189400
106	8	0	-4.957000	3.890800	1.701800
107	1	0	-5.594000	3.594100	1.047400
108	8	0	-0.500800	4.116800	3.393700
109	6	0	-4.173900	2.205200	-0.525100
110	1	0	-5.177300	2.605200	-0.391600
111	1	0	-3.811000	2.515800	-1.505100
112	1	0	-4.227300	1.116900	-0.493200
113	6	0	-3.213800	4.902100	3.701500
114	1	0	-2.541400	4.862600	4.557500
115	1	0	-3.249600	5.923700	3.323300
116	1	0	-4.205200	4.611000	4.047900
117	6	0	2.938900	4.137000	4.601800
118	1	0	3.330400	3.311400	4.086600

Electronic spatial extent (au): <R**2>= 89797.7146
Charge= 0.0000 electrons
Dipole moment (field-independent basis, Debye):
X= -0.7873 Y= -0.4734 Z= -1.5009 Tot= 1.7597
Quadrupole moment (field-independent basis, Debye-Ang):
XX= -370.9381 YY= -382.2564 ZZ= -427.0254
XY= -0.0427 XZ= 53.9961 YZ= -8.8848
Traceless Quadrupole moment (field-independent basis, Debye-Ang):
XX= 22.4686 YY= 11.1502 ZZ= -33.6188
XY= -0.0427 XZ= 53.9961 YZ= -8.8848
Octapole moment (field-independent basis, Debye-Ang**2):
XXX= 1118.3800 YYY= -1486.3763 ZZZ= -6292.8028 XYY= 311.4653
XXY= -516.0856 XXZ= -2015.1505 XZZ= 792.4787 YZZ= -651.0548
YYZ= -1934.7638 XYZ= -11.3018
Hexadecapole moment (field-independent basis, Debye-Ang**3):
XXXX= -18366.7180 YYYY= -20831.5712 ZZZZ= -81938.2861 XXXY= -2655.5692
XXXZ= 3855.8644 YYYX= -1681.5733 YYYZ= -6508.2209 ZZZX= 5882.3388
ZZZY= -9602.7329 XXYY= -6453.2554 XXZZ= -16289.6014 YYZZ= -16551.9441
XXYZ= -2494.6388 YYXZ= 1056.2804 ZZXY= -1072.6861
N-N= 1.328978579053D+04 E-N=-3.433533215860D+04 KE= 3.307601846268D+03
1|1|UNPC-HP-PC|SP|RB3LYP TD-FC|6-31G|C56H46N2O14|HP|13-Jun-2021|0||# t d b3lyp/6-31g nosymm geom=connectivity||Title Card Required||0,1|C,0,-2.6691,-0.2708,2.2642|C,0,-1.2073,-0.177,2.7478|C,0,-0.9417,0.5945,3.9688|C,0,-1.989,1.1892,4.557|C,0,-3.3592,1.0954,4.1233|C,0,-3.7343,0.396,3.0408|C,0,0.3466,0.7896,4.6507|C,0,-1.9311,1.9789,5.6728|C,0,-0.6298,2.2411,6.3049|C,0,0.4075,1.5929,5.7569|C,0,1.7642,1.6206,6.242|C,0,2.1395,2.3366,7.3148|C,0,1.101,3.1457,7.9846|C,0,-0.3489,3.1037,7.4594|C,0,1.5763,0.3061,4.4018|H,0,1.8283,-0.3341,3.6092|C,0,-3.1771,2.3756,5.9863|H,0,-3.4326,2.9971,6.7923|N,0,-4.1016,1.829,5.0619|H,0,-5.0412,2.169,4.9154|N,0,2.4842,0.7713,5.3861|H,0,3.4894,0.7689,5.2888|O,0,1.3841,3.8488,8.9542|O,0,-1.2283,3.7803,7.9897|O,0,-0.3001,-0.699,2.1025|O,0,-2.9347,-0.8784,1.2275|C,0,-5.1987,0.2907,2.6599|H,0,-5.4457,1.0619,1.9321|H,0,-5.402,-0.6885,2.2273|H,0,-5.8245,0.4171,3.5438|C,0,3.5704,2.3009,7.8195|H,0,3.8993,3.307,8.0776|H,0,3.6272,1.6743,8.7086|H,0,4.2337,1.8984,7.0535|C,0,-2.394,-3.5258,3.1934|C,0,-1.6332,-2.9705,4.243|C,0,-2.282,-2.2402,5.2589|C,0,-3.6821,-2.0896,5.2543|C,0,-4.4432,-2.7014,4.2325|C,0,-3.792,-3.3362,3.1533|C,0,-4.2828,-1.3375,6.3704|C,0,-

3.4368,-0.9948,7.5176|C,0,-2.0376,-1.0792,7.3603|C,0,-1.111,-0.5624,8.
2925|C,0,-0.465,1.0674,9.9914|H,0,-0.7,1.919,10.5603|C,0,0.8206,0.5085
,10.066|C,0,1.1472,-0.5926,9.2497|C,0,0.1879,-1.1047,8.3588|H,0,0.4413
,-1.93,7.7607|O,0,1.7305,1.0823,10.8888|H,0,2.6247,0.7362,10.9416|C,0,
2.5242,-1.2309,9.3025|H,0,3.2085,-0.675,8.6629|H,0,2.9016,-1.2341,10.3
252|H,0,2.4693,-2.2611,8.9506|C,0,-4.0778,-0.9231,8.8941|H,0,-3.3536,-
1.1865,9.6648|H,0,-4.4533,0.0847,9.071|H,0,-4.9085,-1.6271,8.9514|O,0,
-5.4128,-0.854,6.3019|O,0,-5.796,-2.7699,4.3244|H,0,-6.3093,-3.2171,3.
6469|O,0,-1.7806,-4.2808,2.2471|H,0,-2.2919,-4.6867,1.5428|O,0,-1.5408
,-1.6928,6.2567|C,0,-4.6052,-3.8521,1.9709|H,0,-4.9766,-4.8519,2.1946|
H,0,-5.4482,-3.1895,1.776|H,0,-3.9966,-3.8863,1.0676|C,0,-0.1254,-3.19
62,4.3033|H,0,0.0775,-4.1578,4.7746|H,0,0.3006,-3.1902,3.3004|H,0,0.36
6,-2.4085,4.8729|C,0,-1.4098,0.5611,9.0862|H,0,-2.3006,1.0947,8.936|C,
0,-3.6554,3.5167,1.6132|C,0,-2.7438,3.969,2.5896|C,0,-1.3781,3.6413,2.
4713|C,0,-0.9207,2.8291,1.4152|C,0,-1.8478,2.3371,0.4677|C,0,-3.2101,2

.6972,0.5519|C,0,0.5358,2.6133,1.3209|C,0,1.4135,3.4294,2.162|C,0,0.85

11,4.0359,3.3031|C,0,1.6245,4.5769,4.3539|C,0,3.7125,4.7299,5.6097|H,0

,4.701,4.4071,5.7604|C,0,3.1431,5.6773,6.4744|C,0,1.7929,6.0429,6.3111

|C,0,1.0517,5.5096,5.2419|H,0,0.0633,5.8336,5.0974|O,0,3.9006,6.1896,7

.4731|H,0,3.5276,6.8246,8.0892|C,0,1.1292,7.0064,7.2774|H,0,0.0629,7.0

799,7.0635|H,0,1.2591,6.6494,8.2991|H,0,1.5831,7.9924,7.1775|C,0,2.717

4,3.9346,1.5651|H,0,3.0043,4.8794,2.0266|H,0,3.5035,3.1958,1.7207|H,0,
2.5929,4.1009,0.4946|O,0,1.0424,1.7527,0.6014|O,0,-1.4466,1.5285,-0.54
6|H,0,-2.081,1.2031,-1.1894|O,0,-4.957,3.8908,1.7018|H,0,-5.594,3.5941
,1.0474|O,0,-0.5008,4.1168,3.3937|C,0,-4.1739,2.2052,-0.5251|H,0,-5.17
73,2.6052,-0.3916|H,0,-3.811,2.5158,-1.5051|H,0,-4.2273,1.1169,-0.4932
|C,0,-3.2138,4.9021,3.7015|H,0,-2.5414,4.8626,4.5575|H,0,-3.2496,5.923
7,3.3233|H,0,-4.2052,4.611,4.0479|C,0,2.9389,4.137,4.6018|H,0,3.3304,3.3114,4.0866||Version=IA32W-G09RevD.01|HF=-**3323.2000792**|RMSD=3.400e-009|PG=C01 [X(C56H46N2O14)]||@

SACRED COWS MAKE GREAT HAMBURGERS -- ROBERT REISNER

Job cpu time: 3 days 21 hours 51 minutes 54.0 seconds.

File lengths (MBytes): RWF= 1179 Int= 0 D2E= 0 Chk= 90 Scr= 1

Normal termination of Gaussian 09 at Sun Jun 13 09:04:20 2021.