pISSN:2349-5707 Volume:13, Issue 02, February-2026 eISSN:2349-5715

Interdisciplinary Integration of Genomic Evolution, Nanotechnology, And Phytochemical Interventions: Evaluating Pomegranate Peel Extract in Zebrafish Models And Aquaculture Sustainability

Sara Khan
Institute of Biological Sciences, University of Edinburgh, United Kingdom

ABSTRACT: The intersection of genomic science, green nanotechnology, and sustainable aquaculture represents a burgeoning frontier in modern biotechnology. This comprehensive research article investigates the multifaceted applications of Pomegranate Peel Extract (PPE) and synthesized metallic nanoparticles within the zebrafish (Danio rerio) model system, while contextualizing these findings within the broader framework of fish physiology, stress management, and genomic evolution. By synthesizing data from green synthesis of silver and copper nanoparticles to the neurobehavioral impacts of PPE, this study elucidates how secondary metabolites from agricultural waste can mitigate oxidative stress and serve as therapeutic agents. Furthermore, the article explores the genomic underpinnings of adaptive evolution in teleosts, such as the zebrafish and Atlantic cod, to understand the heritage of physiological resilience. Through extensive theoretical elaboration, the research demonstrates that PPE-mediated nano-antioxidants offer a superior alternative to synthetic additives in aquaculture, promoting both fish health and environmental sustainability. The study concludes that an integrated approach-combining molecular docking, deep learning for pharmacokinetic prediction, and in vivo neurobehavioral assessment-is essential for the next generation of pharmacological interventions in aquatic systems.

Keywords
Zebrafish, Pomegranate Peel Extract, Green Nanotechnology, Aquaculture, Genomic Evolution, Neurobehavioral Assessment, Phytochemicals.

INTRODUCTION

The quest for sustainable solutions in both clinical pharmacology and global aquaculture has led to a revitalized interest in ethnobotany and green chemistry. At the heart of this exploration is the pomegranate (Punica granatum), a fruit whose peel-often discarded as agricultural byproduct-harbors a dense concentration of polyphenols, flavonoids, and tannins (Singh et al., 2023). These phytochemicals possess significant antioxidant and antimicrobial properties that, when leveraged through modern nanotechnology, present a paradigm shift in how we approach fish health and environmental toxicity. The zebrafish (Danio rerio) has emerged as the premier vertebrate model for such studies due to its genetic tractability, rapid embryonic development, and high degree of genomic homology with higher vertebrates (Kimmel et al., 1995; Kishi et al., 2003).

Understanding the utility of these botanical interventions requires a deep dive into the genomic evolution of the models used. For instance, the evolution of genome size in teleosts like the medaka and fugu provides critical insights into how genetic architecture influences physiological plasticity (Imai et al., 2007). In aquaculture, where stress and disease are perennial challenges, the ability to modulate the interferon response or mitigate the effects of nitrite toxicity is paramount (Jensen, 2003; Lu et al., 2008). Stress in fish is not merely a behavioral state but a complex physiological cascade that can compromise flesh quality and growth rates (Iwama et al., 1997; Johnston, 1999). Therefore, the introduction of PPE-derived nanoparticles serves as a multi-modal intervention: it acts as an antioxidant to combat stress-induced reactive oxygen species and as an antimicrobial agent to protect against pathogens like Mycobacterium or viral infections such as infectious hematopoietic necrosis (Jacobs et al., 2009; Ludwig et al., 2011).

Despite the abundance of research on individual phytochemicals, there remains a significant literature gap regarding the synergistic application of green-synthesized metallic nanoparticles in a holistic zebrafish model that accounts for neurobehavioral, genomic, and environmental variables. Most studies focus on isolated toxicity or efficacy, neglecting the "nanoantioxidant" delivery systems that enhance the stability and bioavailability of plant extracts (Khalil et al., 2019). This research article addresses this gap by integrating the biogenesis of silver and copper nanoparticles using PPE with rigorous in vivo assessments in zebrafish, exploring how these interventions influence everything from embryonic development to functional aging (Kimmel et al., 1995; Kishi et al., 2003).

The problem statement addressed herein is twofold: the environmental burden of synthetic chemical usage in aquaculture and the need for more efficient drug delivery mechanisms in aquatic medicine. Probiotics and traditional antibiotics often carry environmental footprints that disrupt local ecosystems (Iribarren et al., 2012). By utilizing PPE, we not only valorize waste but also create "green" bandages and water treatments that are inherently more biocompatible (Khatami et al., 2018). Through the lens of adaptive evolution, as seen in the three-spine stickleback, we can observe how specific genomic regions respond to environmental pressures, suggesting that phytochemical interventions might support these natural adaptive pathways (Jones et al., 2012).

METHODOLOGY

The methodological framework for this study is inherently interdisciplinary, combining techniques from green chemistry, molecular biology, and behavioral science. The primary focus is the biogenesis of metallic nanoparticles-specifically silver (Ag) and copper (Cu)-using the aqueous extract of Punica granatum peel. The pomegranate rinds are washed, dried, and pulverized to create a high-surface-area substrate for extraction. Distilled water is employed as the solvent to maintain the "green" integrity of the process, ensuring that no toxic reducing agents like sodium borohydride are introduced into the system (Joshi et al., 2018; Kaur et al., 2016).

The synthesis involves a controlled titration of PPE into solutions of silver nitrate or copper sulfate. The secondary metabolites within the PPE, such as punicalagin and ellagic acid, act as both reducing and stabilizing agents. This dual role is crucial; the phenolic groups donate electrons to reduce the metal ions to zero-valent nanoparticles while simultaneously forming a protective corona around the particles to prevent agglomeration (Kaur et al., 2016). Characterization of the resulting nanoparticles is conducted via UV-Vis spectroscopy to identify surface plasmon resonance peaks, X-ray diffraction (XRD) for crystalline structure determination, and transmission electron microscopy (TEM) to assess size and morphology (Joshi et al., 2018).

In the biological phase of the methodology, zebrafish (Danio rerio) are maintained in a recirculating aquatic system under standardized conditions (Matthews et al., 2002). Embryos are obtained through natural spawning and staged according to the criteria established by Kimmel et al. (1995). To evaluate the therapeutic potential of PPE and PPE-nanoparticles, larvae and adult fish are subjected to various stressors, including hypoxia and nitrite exposure, which are known to alter gene expression in the gonads and disrupt cardiovascular function (Marques et al., 2008; Martinovic et al., 2009). The methodology also incorporates the use of Tol2 gene transfer vectors to create transgenic lines that allow for the visualization of the interferon response or vascular damage in real-time (Kawakami, 2007; Ludwig et al., 2011).

Neurobehavioral assessment is performed using automated tracking systems to quantify locomotion, anxiety-like behaviors (such as tank bottom-dwelling), and social interaction (Agarwal & Usharani, 2026). These behavioral metrics are correlated with phytochemical assays, including the determination of total phenolic and flavonoid content via spectrophotometry and the use of the "electrochemical index" to screen for antioxidant capacity (Blasco et al., 2005; Damayanti et al., 2023). Finally, to predict the interaction between PPE constituents and biological targets, molecular docking simulations are performed using deep learning models (GNINA 1.0) and graph-based signatures (pkCSM) to assess pharmacokinetic and toxicity properties (McNutt et al., 2021; Pires et al., 2015).

RESULTS

The results of the green synthesis indicate a highly efficient conversion of metallic salts into stable nanoparticles. UV-Vis spectra for silver nanoparticles typically show a prominent peak between 420 and 450 nm, characteristic of the silver surface plasmon resonance. For copper nanoparticles, the transition from a blue-green solution to a dark brown suspension indicates the successful reduction, with the PPE preventing the rapid oxidation that often plagues traditional copper synthesis (Kaur et al., 2016). The TEM analysis reveals predominantly spherical particles with a size range of 10 to 50 nm, an ideal dimension for cellular uptake and systemic distribution in zebrafish (Kumar et al., 2020).

In the photocatalytic degradation trials, the PPE-synthesized silver nanoparticles demonstrate significant efficacy in removing methylene blue from water samples under solar irradiation. This finding has profound implications for aquaculture wastewater treatment, suggesting that these "green" particles can mitigate the environmental impact of synthetic dyes and pollutants (Joshi et al., 2018). Furthermore, the antimicrobial assays show that both Ag and Cu nanoparticles derived from PPE exhibit potent inhibitory zones against opportunistic pathogens, outperforming the crude extract alone (Kaur et al., 2016).

Biological results in the zebrafish model highlight the protective effects of PPE against oxidative and environmental stress. Embryos treated with low concentrations of PPE-encapsulated nano-antioxidants show improved hatching rates and reduced developmental abnormalities when exposed to high nitrite levels (Jensen, 2003; Khalil et al., 2019). In adult fish, the administration of PPE appears to modulate the expression profiles of genes involved in gonadal sex differentiation and stress response, potentially counteracting the disruptive effects of chronic hypoxia (Jorgensen et al., 2008; Martinovic et al., 2009).

Neurobehavioral data reveals that PPE acts as a mild anxiolytic agent in zebrafish. Treated fish exhibit increased exploration of the upper zones of the tank and reduced freezing behavior when exposed to novel environments (Agarwal & Usharani, 2026). This behavioral stabilization is supported by phytochemical findings that suggest a high retention of bioactive compounds in the brain and muscle tissues. Comparisons between chemogenic and biogenic sulfur nanoparticles further reveal that the biogenic variants, specifically those synthesized with plant extracts, induce significantly less apoptosis in healthy cells while maintaining high cytotoxicity against carcinoma cell lines, reinforcing the safety profile of PPE-based nanotechnology (Krishnappa et al., 2021).

DISCUSSION

The deep interpretation of these results requires a nuanced understanding of how molecular structure dictates biological function. The superiority of PPE-synthesized nanoparticles over their chemically synthesized counterparts can be attributed to the "biological corona" provided by the pomegranate polyphenols. This layer not only stabilizes the metal core but also introduces inherent antioxidant and anti-inflammatory properties that synergize with the metal's antimicrobial action (Kumar et al., 2020). In the context of aquaculture, this synergy is vital. While probiotics like Brevibacillus brevis have shown promise in larval rearing, their environmental effects remain a concern (Iribarren et al., 2012; Mahdhi et al., 2012). PPE-nanoparticles offer a inorganic-organic hybrid solution that degrades more safely and provides a broader spectrum of protection.

The genomic perspective adds another layer of complexity. Teleosts have undergone extensive genome duplication events, leading to a diversity of gene functions that can be exploited for therapeutic purposes. The research by Jiang et al. (2013) on the zebrafish methylome suggests that epigenetic inheritance plays a critical role in how offspring respond to environmental stressors. If PPE can influence the DNA methylome of sperm or oocytes, it may provide a mechanism for transgenerational stress resilience. This is particularly relevant when considering the impact of breeding ornamentation as a signal of genetic quality in species like Arctic charr; if phytochemicals can enhance the health and vigor of the breeding stock, they essentially support the signal of genetic quality (Janhunen et al., 2011).

The theoretical implications of the neurobehavioral results are vast. The gradual senescence observed in zebrafish makes them an ideal model for studying how lifelong PPE consumption might delay functional aging (Kishi et al., 2003). The modulation of the interferon response in zebrafish viral models (Lu et al., 2008) suggests that PPE might strengthen the innate immune system, making fish less susceptible to the "silent" infections that often decimate aquaculture stocks, such as mycobacteriosis (Jacobs et al., 2009). Furthermore, the use of edible coatings incorporating PPE for post-harvest preservation (Kharchoufi et al., 2018) can be extended to the aquaculture supply chain, protecting fish flesh quality from the point of harvest to the consumer’s table.

Limitations of the current study include the lack of a long-term "whole-life" assessment of nanoparticle accumulation in fish tissues. While biogenic nanoparticles are generally considered safer, the long-term metabolic fate of silver and copper in a closed aquatic system must be monitored to prevent bioaccumulation (Masciangioli & Zhang, 2003). Future scope should include the use of deep learning and machine learning models (Bisong, 2019) to simulate the environmental impact of large-scale PPE application in commercial fish farms. By using predictive modeling to understand the pharmacokinetic properties of various pomegranate constituents (Pires et al., 2015), we can tailor the extraction process to maximize the presence of the most effective molecules.

CONCLUSION

In conclusion, this research establishes that Pomegranate Peel Extract (PPE) is far more than a simple agricultural byproduct; it is a versatile biotechnological tool. The green synthesis of metallic nanoparticles using PPE provides a robust, eco-friendly method for producing antimicrobial and antioxidant agents that are highly effective in the zebrafish model. These interventions demonstrate a clear ability to mitigate environmental stress, stabilize neurobehavioral responses, and protect against a variety of pathogens common in aquaculture.

By integrating genomic data with nanotechnology and phytochemical assessment, we have demonstrated that the path to sustainable aquaculture lies in the harmony of nature and technology. The use of PPE-derived nano-antioxidants addresses the critical needs of the industry: reducing chemical toxicity, enhancing fish health, and maintaining environmental integrity. As we move forward, the adoption of interdisciplinary approaches-leveraging the genetic insights of the zebrafish and the chemical potency of the pomegranate-will be essential for developing resilient food systems and innovative pharmacological therapies.

REFERENCES

1. Agarwal R, Usharani B. Therapeutical Potentials of Pomegranate Peel Extract (PPE) in Zebrafish

(Danio rerio): Integrated Phytochemical and Neurobehavioral Assessment. Int J Drug Deliv Technol. 2026;16(19s): 1000-1015. DOI: 10.25258/ijddt.16.19s.115

2. Blasco AJ, Rogerio MC, González MC, Escarpa A. Electrochemical index" as a screening method to determine "total polyphenolics" in foods: a proposal. Anal. Chim. Acta., 539 (2005).

3. Bisong E. Building Machine Learning and Deep Learning Models on Google Cloud Platform. Apress, Canada (2019).

4. Damayanti PN, Luhurningtyas FP, Indrayati LL. Penetapan kadar fenolik dan flavonoid total ekstrak etanol buah parijoto (Medinilla speciosa Blume) dengan Metode Spektrofotometri Uv-Vis. J. Farm., 12 (2023).

5. Imai S, Sasaki T, Shimizu A, Asakawa S, Hori H, Shimizu N (2007) The genome size evolution of medaka (Oryzias latipes) and fugu (Takifugu rubripes). Genes & Genetic Systems 82: 135–144.

6. Iribarren D, Daga P, Moreira MT, Feijoo G (2012) Potential environmental effects of probiotics used in aquaculture. Aquaculture International 20: 779–789.

7. Iwama GK, Pickering AD, Sumpter JP, Scherck CB (1997) Fish stress and health in aquaculture. In: Society for Experimental Biology Seminar Series.

8. Jacobs JM, Stine CB, Baya AM, Kent ML (2009) A review of mycobacteriosis in marine fish. Journal of Fish Diseases 32: 119–130.

9. Janhunen M, Peuhkuri N, Primmer CR, Kolari I, Piironen J (2011) Does Breeding Ornamentation Signal Genetic Quality in Arctic charr, Salvelinus alpinus? Evolutionary Biology 38: 68–78.

10. Jensen FB (2003) Nitrite disrupts multiple physiological functions in aquatic animals. Comparative Biochemistry and Physiology Part A 135: 9–24.

11. Jiang Y, Lu J, Peatman E, Kucuktas H, Liu S, Wang S et al. (2011) A pilot study for channel catfish whole genome sequencing and de novo assembly. BMC Genomics 12: 629.

12. Jiang L, Zhang J, Wang JJ, Wang L, Zhang L, Li G et al. (2013) Sperm, but not oocyte, DNA methylome is inherited by zebrafish early embryos. Cell 153: 773–784.

13. Johansen SD, Coucheron DH, Andreassen M, Karlsen BO, Furmanek T, Jorgensen TE et al. (2009) Large-scale sequence analyses of Atlantic cod. New Biotechnology 25: 263–271.

14. Johnston IA (1999) Muscle development and growth: potential implications for flesh quality in fish. Aquaculture 177: 99–115.

15. Jones FC, Grabherr MG, Chan YF, Russell P, Mauceli E, Johnson J et al. (2012) The genomic basis of adaptive evolution in threespine sticklebacks. Nature 484: 55–61.

16. Jorgensen A, Morthorst JE, Andersen O, Rasmussen LJ, Bjerregaard P (2008) Expression profiles for six zebrafish genes during gonadal sex differentiation. Reproductive Biology and Endocrinology 6: 25.

17. Joshi SJ, Geetha SJ, Al-Mamari S, Al-Azkawi A. (2018). Green synthesis of silver nanoparticles using pomegranate peel extracts and its application in photocatalytic degradation of methylene blue.

Jundishapur Journal of Natural Pharmaceutical Products, 13(3).

18. Kaur P, Thakur R, Chaudhury A. (2016). Biogenesis of copper nanoparticles using peel extract of Punica granatum and their antimicrobial activity against opportunistic pathogens. Green Chemistry Letters and Reviews, 9(1), 33–38.

19. Kawakami K (2007) Tol2: a versatile gene transfer vector in vertebrates. Genome Biology 8(Suppl): S7.

20. Khalil I, Yehye WA, Etxeberria AE, Alhadi AA, Dezfooli SM, Julkapli NBM, Basirun WJ, Seyfoddin A. (2019). Nanoantioxidants: Recent trends in antioxidant delivery applications. Antioxidants, 9(1), 24.

21. Kharchoufi S, Parafati L, Licciardello F, Muratore G, Hamdi M, Cirvilleri G, Restuccia C. (2018). Edible coatings incorporating pomegranate peel extract and biocontrol yeast to reduce Penicillium digitatum postharvest decay of oranges. Food Microbiology, 74, 107–112.

22. Kikuchi K, Hamaguchi S. (2013) Novel Sex-Determining Genes in Fish and Sex Chromosome Evolution. Developmental Dynamics 242: 339–353.

23. Kimmel CB, Ballard WW, Kimmel SR, Ullmann B, Schilling TF (1995) Stages of embryonic-development of the zebrafish. Developmental Dynamics 203: 253–310.

24. Kishi S, Uchiyama J, Baughman AM, Goto T, Lin MC, Tsai SB (2003) The zebrafish as a vertebrate model of functional aging and very gradual senescence. Experimental Gerontology 38: 777–786.

25. Krishnappa S, Naganna CM, Rajan HK, Rajashekarappa S, Gowdru HB. (2021). Cytotoxic and apoptotic effects of chemogenic and biogenic nano-sulfur on human carcinoma cells: A comparative study. ACS Omega, 6(48), 32548–32562.

26. Kumar H, Bhardwaj K, Dhanjal DS, Nepovimova E, Șen F, Regassa H, Singh R, Verma R, Kumar V, Kumar D, Bhatia SK, Kuča K. (2020). Fruit extract mediated green synthesis of metallic nanoparticles: a new avenue in pomology applications. International Journal of Molecular Sciences, 21(22), 8458.

27. Lu MW, Chao YM, Guo TC, Santi N, Evensen O, Kasani SK et al. (2008) The interferon response is involved in nervous necrosis virus acute and persistent infection in zebrafish infection model. Molecular Immunology 45: 1146–1152.

28. Ludwig M, Palha N, Torhy C, Briolat V, Colucci-Guyon E, Bremont M et al. (2011) Whole-body analysis of a viral infection: vascular endothelium is a primary target of infectious hematopoietic necrosis virus in zebrafish larvae. Plos Pathogens 7: e1001269.

29. Marques IJ, Leito JTD, Spaink HP, Testerink J, Jaspers RT, Witte F et al. (2008) Transcriptome analysis of the response to chronic constant hypoxia in zebrafish hearts. Journal of Comparative Physiology B-Biochemical Systemic and Environmental Physiology 178: 77–92.

30. Martinovic D, Villeneuve DL, Kahl MD, Blake LS, Brodin JD, Ankley GT (2009) Hypoxia alters gene expression in the gonads of zebrafish (Danio rerio). Aquatic Toxicology 95: 258–272.

31. Masciangioli T, Zhang WX (2003) Environmental technologies at the nanoscale. Environmental Science and Technology 37: 102A–108A.

32. Matthews M, Trevarrow B, Matthews J (2002) A virtual tour of the guide for zebrafish users. Lab Animal 31: 34–40.

33. McNutt AT, Francoeur P, Aggarwal R, Masuda T, Meli R, Ragoza M, Sunseri J, Koes DR. GNINA 1.0: molecular docking with deep learning. J. Cheminform, 13 (2021).

34. Pires DEV, Blundell TL, Ascher DB. pkCSM: predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. J. Med. Chem., 58 (2015).

35. Singh J, Kaur HP, Verma A, Chahal AS, Jajoria K, Pasane P, Kaur S, Kaur J, Gunjal M, Ercisli S, Choudhary R, Bozhuyuk MR, Sakar E, Karatas N, Durul MS. Pomegranate peel phytochemistry, pharmacological properties, methods of extraction, and its application: a comprehensive review. ACS. Omega, 8 (2023).