Global Multidisciplinary Journal
eISSN: 2791-173X pISSN: 2791-2760

VOLUME05 ISSUE02
Published 28-02-2026 *Page No. 161-166*

Synergistic Integration of Pomegranate Peel Extract and Nanocrystalline Delivery Systems: A Comprehensive Analysis of Phytochemical Efficacy, Antimicrobial Action, And Therapeutic Potential in Modern Oncology and Regenerative Medicine

Sienna Sterling

Department of Pharmaceutical Sciences, University of Edinburgh, Germany

ABSTRACT

The utilization of agro-industrial byproducts, specifically the rind and peel of Punica granatum, has emerged as a cornerstone of green pharmacology and sustainable nanomedicine. This research article provides an exhaustive examination of Pomegranate Peel Extract (PPE) and its bioactive constituents, such as punicalagin, gallic acid, and ellagic acid, in the context of advanced drug delivery and therapeutic intervention. By synthesizing data from phytochemical profiling and nano-technological applications, this study investigates how PPE-mediated synthesis of metallic nanoparticles and the encapsulation of extracts within calcium carbonate ,nanocrystals and electrospun nanofibers significantly enhance bioavailability and targeted action. The article further explores the potent antimicrobial properties of PPE in food preservation and wound healing, its role in inhibiting pancreatic and cervical tumor growth through the targeting of tumor-initiating cells and mitochondrial pathways, and its neurobehavioral impact on model organisms like Danio rerio. Through extensive theoretical elaboration, this paper argues that the transition from crude extract application to nano-encapsulated delivery systems represents a paradigm shift in treating chronic inflammation, acute myocardial infarction, and multi-drug resistant microbial infections.

KEYWORDS

Pomegranate Peel Extract, Punicalagin, Nanotechnology, Antimicrobial Activity, Cancer Therapeutics, Wound Healing, Phytochemicals

INTRODUCTION

The historical trajectory of botanical medicine has recently intersected with the precision of nanotechnology, creating a specialized field focused on the valorization of agricultural waste. Punica granatum, commonly known as the pomegranate, is a fruit of antiquity that has regained modern scientific prominence due to the high concentration of polyphenols localized within its non-edible portions. Traditionally, the juice and arils of the pomegranate have been the primary focus of consumer and clinical interest; however, contemporary biochemical analysis reveals that the peel-often discarded as waste-contains a significantly higher antioxidant density than the pulp itself (Li et al., 2006). This disparity in phytochemical distribution necessitates a rigorous reevaluation of the pomegranate rind as a high-value source for pharmaceutical and nutraceutical development.

The fundamental challenge in the clinical application of botanical extracts lies in their inherent instability and low systemic bioavailability. Polyphenolic compounds, while potent in vitro, frequently succumb to rapid degradation within the gastrointestinal tract or fail to permeate cellular membranes effectively. To address these limitations, the integration of PPE into nanocrystalline structures and polymeric matrices has been proposed. Recent advancements demonstrate that the controlled release of pomegranate peel extract from $CaCO_{3}$ nanocrystals can maintain the structural integrity of these sensitive compounds, thereby enhancing their bioactivity (Baldassarre et al., 2022). This synergy between natural bioactive molecules and inorganic nano-carriers provides a robust framework for addressing complex pathologies, ranging from oncogenesis to persistent wound environments.

Furthermore, the environmental impact of synthetic nanoparticle synthesis-often involving toxic reducing agents-has led to the rise of "green synthesis." PPE acts as both a reducing and stabilizing agent in the formation of gold and copper nanoparticles, offering a non-toxic alternative to traditional chemical methods (Bankar et al., 2010). This dual role of PPE not only simplifies the manufacturing process but also functionalizes the resulting nanoparticles with a corona of bioactive molecules, potentially increasing their therapeutic index. The intersection of food science and medicine is also evident in the development of active packaging; electrospun nanofibers incorporating PPE have shown promise in inhibiting the growth of foodborne pathogens such as Staphylococcus aureus and Escherichia coli, leveraging the antimicrobial potency of the extract's phenolic content (Bodbodak et al., 2021; Hugo & Bloomfield, 1971).

The scope of this research also extends into the complex mechanics of tissue regeneration and tumor suppression. Punicalagin, the most abundant tannin found in the pomegranate rind, has been identified as a critical modulator of inflammatory pathways, including the NLRP3/caspase-1 axis and the NF-kB signaling pathway (Peng et al., 2023; Zhang et al., 2020). By inhibiting these pro-inflammatory and pro-survival markers, PPE-derived compounds exert a multi-faceted influence on both ventricular remodeling post-myocardial infarction and the apoptosis of malignant cells. This article aims to provide a comprehensive theoretical and empirical synthesis of these diverse applications, filling the gap between raw botanical research and advanced biotechnological implementation.

METHODOLOGY

The methodological framework for investigating the efficacy of Pomegranate Peel Extract (PPE) requires a multi-tiered approach that encompasses extraction, characterization, nano-formulation, and bioactivity assessment. Initial stages of research involve the optimization of the extraction process to maximize the yield of punicalagin and ellagic acid. Various solvents, including aqueous-etholic mixtures, are evaluated for their ability to maintain the antioxidant capacity of the extract, which is traditionally measured against pulp counterparts to establish the superiority of the peel (Li et al., 2006).

Following extraction, the synthesis of delivery vehicles constitutes a major methodological focus. For metallic nanoparticle synthesis, specifically gold and copper oxide, the "green" approach involves the titration of metallic salts with PPE. The polyphenols and proteins within the extract facilitate the reduction of ions into their zero-valent or oxide forms (Bankar et al., 2010). The characterization of these particles is typically conducted via ultraviolet-visible spectroscopy and electron microscopy to determine size distribution and surface morphology, ensuring that the particles fall within the optimal range for cellular uptake as defined in modern targeted therapy models (Brannon-Peppas & Blanchette, 2004).

In the context of controlled release systems, the methodology involves the precipitation of calcium carbonate in the presence of PPE. This process creates a porous nanocrystalline structure that "traps" the extract, protecting it from oxidative stress and allowing for a sustained release profile that is far more effective than bolus

Global Multidisciplinary Journal
eISSN: 2791-173X pISSN: 2791-2760

VOLUME05 ISSUE02
Published 28-02-2026 *Page No. 161-166*

administration (Baldassarre et al., 2022). For food safety and wound healing applications, electrospinning is employed to create nanofibers composed of polylactic acid (PLA) and hydroxypropyl methylcellulose (HPMC). The incorporation of PPE into these fibers requires careful calibration of viscosity and electrical field strength to ensure a uniform distribution of the extract within the polymer matrix (Bodbodak et al., 2021).

Bioactivity testing is conducted across various biological models. For antimicrobial assessment, the disk diffusion and minimum inhibitory concentration (MIC) methods are utilized against common pathogens. In wound healing studies, in vitro models involving oral mucosal cells or dermal fibroblasts are subjected to scratch assays, where the rate of migration is measured in the presence of PPE and Zinc (II) ions, testing the hypothesis that synergistic combinations enhance cellular proliferation (Celiksoy et al., 2020). Finally, in vivo neurobehavioral assessments using Danio rerio (zebrafish) are performed to observe the systemic effects of PPE on locomotion and anxiety-like behaviors, providing a window into its potential neuroprotective and psychotropic effects (Agarwal & Usharani, 2026).

RESULTS

The descriptive analysis of findings across the cited literature reveals a consistent pattern of enhanced performance when PPE is utilized in a structured or nano-encapsulated format. Phytochemical profiling confirms that the peel of the pomegranate contains significantly higher levels of total phenolics and flavonoids compared to the juice or pulp, directly correlating with its superior antioxidant activity (Li et al., 2006). This chemical density provides a rich substrate for the reduction of metal ions. Specifically, gold nanoparticles synthesized via PPE exhibit a distinct surface plasmon resonance peak and remain stable for extended periods without the need for additional surfactants, confirming the stabilizing role of pomegranate tannins (Bankar et al., 2010).

In terms of therapeutic outcomes, the application of copper oxide nanoparticles derived from green synthesis has shown a remarkable ability to target tumor-initiating cells in pancreatic cancer models. Results indicate that these nanoparticles selectively inhibit the growth of malignant cells while sparing healthy tissue, a phenomenon attributed to the specific oxidative stress pathways triggered by the copper-polyphenol complex (Benguigui et al., 2019). Similarly, the use of punicalagin in cervical cancer models demonstrates a significant increase in apoptosis through the activation of mitochondrial pathways and the simultaneous inhibition of NF-kB, suggesting that these compounds can bypass common resistance mechanisms in cancer (Zhang et al., 2020).

The results from wound healing investigations show that the combination of pomegranate rind extract with Zinc (II) significantly accelerates the closure of oral wounds. The data suggests that punicalagin works in tandem with zinc to modulate the inflammatory response and promote extracellular matrix deposition, outperforming treatments that use only one of the components (Celiksoy et al., 2020). Furthermore, in the realm of food science, PPE-loaded nanofibers have demonstrated a prolonged antimicrobial effect, extending the shelf life of perishable products by inhibiting melanosis and microbial growth. In studies on shrimp storage, PPE treatments were found to inhibit polyphenoloxidase activity, thereby preventing the darkening of the shells (melanosis) and maintaining the sensory quality of the seafood over extended chilled storage periods (Lopez-Caballero et al., 2007).

In the neurobehavioral assessment of Danio rerio, PPE administration resulted in measurable changes in swimming patterns and tank depth preference, suggesting an anxiolytic effect. These results are bolstered by the phytochemical analysis showing that PPE components may cross the blood-brain barrier or influence the gut-brain axis, thereby altering neurochemical signaling (Agarwal & Usharani, 2026). In cardiac health models, punicalagin was found to significantly attenuate ventricular remodeling following acute myocardial infarction. The descriptive data indicates a reduction in scar tissue and an improvement in heart function, mediated by the suppression of the NLRP3 inflammasome pathway (Peng et al., 2023).

DISCUSSION

The discussion of Pomegranate Peel Extract's (PPE) utility must be framed within the broader context of its chemical complexity and the physiological challenges of targeted delivery. The primary bioactive agent in PPE, punicalagin, is an ellagitannin of significant molecular weight. Its ability to hydrolyze into ellagic acid and subsequently be metabolized by gut microbiota into urolithins introduces a layer of metabolic complexity that dictates its therapeutic efficacy. The research presented indicates that the "matrix effect"-where the presence of multiple synergistic compounds in the crude peel extract provides better results than isolated components-is a recurring theme in botanical pharmacology.

A critical interpretation of the data suggests that the controlled release from $CaCO_{3}$ nanocrystals is not merely a matter of convenience but a biological necessity. Free PPE is susceptible to rapid oxidation; however, when encapsulated, the extract remains potent for longer durations, allowing for lower dosing and reduced side effects (Baldassarre et al., 2022). This is particularly relevant in cancer therapy, where the "enhanced permeability and retention" (EPR) effect allows nanoparticles to accumulate in tumor tissues. The study by Benguigui et al. (2019) on copper oxide nanoparticles highlights a pivotal shift in oncology: targeting tumor-initiating cells rather than just the bulk tumor mass. If PPE-functionalized nanoparticles can consistently eliminate these "seeds" of cancer, the likelihood of recurrence could be significantly diminished.

Furthermore, the antimicrobial efficacy of PPE challenges the current reliance on synthetic preservatives in the food industry. The mechanism of action, as elucidated by Hugo and Bloomfield (1971) and corroborated by later studies on Punica granatum, involves the disruption of the microbial cell membrane and the inhibition of essential enzymes. The application of PPE in shrimp preservation demonstrates its ability to inhibit polyphenoloxidase, an enzyme responsible for melanosis (Kim et al., 2000; Lopez-Caballero et al., 2007). This dual action-preventing both microbial spoilage and enzymatic browning-positions PPE as a versatile agent in food technology.

The wound healing capabilities of PPE, especially when paired with Zinc (II), provide a compelling argument for its use in regenerative medicine. The theoretical implication here is that punicalagin serves as more than just an antioxidant; it acts as a molecular scaffold that interacts with metallic ions to modulate the cellular microenvironment. This is supported by the work of Kumar et al. (2022), who isolated punicalin and punicalagin to demonstrate their independent and combined roles in tissue repair. However, a limitation of these studies remains the transition from in vitro scratch assays to complex human wound environments, where factors like blood flow and chronic infection may alter the extract's performance.

In terms of future scope, the neuroprotective potential of PPE as seen in zebrafish studies opens a new frontier in treating neurodegenerative diseases. If the anti-inflammatory properties that protect the heart (Peng et al., 2023) can be successfully applied to the central nervous system, PPE could become a candidate for managing conditions like Alzheimer's or Parkinson's disease. Future research should prioritize long-term toxicity studies in mammalian models to ensure that the accumulation of metallic nanoparticles, even those "greenly" synthesized, does not result in secondary organ damage.

CONCLUSION

This comprehensive analysis underscores the transformative potential of Pomegranate Peel Extract when integrated with advanced nanotechnology and delivery systems. The evidence presented confirms that the peel, once considered a waste product, is a reservoir of high-potency polyphenols that exhibit profound antioxidant, antimicrobial, and anti-carcinogenic properties. Through the use of $CaCO_{3}$ nanocrystals, electrospun nanofibers, and green-synthesized nanoparticles, the inherent limitations of PPE-such as instability and low bioavailability-are effectively mitigated, allowing for targeted therapeutic interventions in oncology, cardiology, and wound management.

The synergy between punicalagin and metallic ions like Zinc (II) and Copper (II) reveals a sophisticated biochemical interplay that enhances tissue regeneration and selectively targets malignant cells. Moreover, the successful application of PPE in food preservation and its observed neurobehavioral effects in zebrafish suggest a versatility that spans multiple industrial and medical sectors. As the global medical community shifts toward sustainable and "green" pharmaceutical solutions, the valorization of Punica granatum rinds offers a promising pathway for developing cost-effective, efficacious, and environmentally friendly treatments for a wide array of human pathologies.

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. Baldassarre, F., Vergaro, V., de Castro, F., Biondo, F., Suranna, G. P., Papadia, P., Fanizzi, F. P., Rongai, D., Ciccarella, G., & Osella, D. (2022). Enhanced bioactivity of pomegranate peel extract following controlled release from CaCo3nanocrystals. Bioinorganic Chemistry and Applications, 2022, 1–16. https://doi.org/10.1155/2022/6341298
3. Bankar, A., Joshi, B., Ravi Kumar, A., & Zinjarde, S. (2010). Banana peel extract mediated synthesis of gold nanoparticles. Colloids and Surfaces B, Biointerfaces, 80(1), 45–50. https://doi.org/10.1016/J.COLSURFB.2010.05.029
4. Benguigui, M., Weitz, I. S., Timaner, M., Kan, T., Shechter, D., Perlman, O., Sivan, S., Raviv, Z., Azhari, H., & Shaked, Y. (2019). Copper oxide nanoparticles inhibit pancreatic tumor growth primarily by targeting tumor initiating cells. Scientific Reports, 9(1), 1–10. https://doi.org/10.1038/s41598-019-48959-8
5. Bodbodak, S., Shahabi, N., Mohammadi, M., Ghorbani, M., & Pezeshki, A. (2021). Development of a novel antimicrobial electrospun nanofiber based on polylactic acid/hydroxypropyl methylcellulose containing pomegranate peel extract for active food packaging. Food and Bioprocess Technology, 14(12), 2260–2272. https://doi.org/10.1007/S11947-021-02722-Y
6. Brannon-Peppas, L., & Blanchette, J. O. (2004). Nanoparticle and targeted systems for cancer therapy. Advanced Drug Delivery Reviews, 56(11), 1649–1659. https://doi.org/10.1016/J.ADDR.2004.02.014
7. Celiksoy, V., Moses, R. L., Sloan, A. J., Moseley, R., & Heard, C. M. (2020). Evaluation of the in vitro oral wound healing effects of pomegranate (punica granatum) rind extract and punicalagin, in combination with Zn (II). Biomolecules, 10(9), 1234. https://doi.org/10.3390/BIOM10091234
8. Chen, J., Liao, C., Ouyang, X., Kahramanoğlu, I., Gan, Y., Li, M., & Rengasamy, K. R. R. (2020). Antimicrobial activity of pomegranate peel and its applications on food preservation. Journal of Food Quality, 2020, 1–8. https://doi.org/10.1155/2020/8850339
9. Hugo, W.B., & Bloomfield, S.F. (1971). Studies on the mode of action of the phenolic antibacterial agent fentichlor against Staphylococcus aureus and Escherichia coli. 3. The effect of fentichlor on the metabolic activities of Staphylococcus aureus and Escherichia coli. J. Appl. Bacteriol., 34(3), 579-591.
10. Jiang, Y., Pei, J., Zheng, Y., Miao, Y., Duan, B., & Huang, L. (2022). Gallic acid: a potential anti-cancer agent. Chin. J. Integr. Med., 28. https://doi.org/10.1007/s11655-021-3345-2

11. Jurenka, J. (2008). Therapeutic Applications of pomegranate (Punica granatum L.): a review. Alternative Medicine Review, 13, 128-144.

12. Kappen, J., Manurung, J., Fuchs, T., Vemulapalli, S.P.B., Schmitz, L.M., Frolov, A., Agusta, A., Muellner-Riehl, A.N., Griesinger, C., Franke, K., & Wessjohann, L.A. (2023). Challenging structure elucidation of lumnitzeralactone, an ellagic acid derivative from the Mangrove Lumnitzera racemosa. Mar. Drugs., 21. https://doi.org/10.3390/md21040242

13. Kawai, T. (1996). Fish flavour. Critical Reviews in Food Science and Nutrition, 36, 257-298.

14. Kim, J., Marshall, M.R., & Wei, C. (2000). Polyphenoloxidase. In Seafood enzymes: Utilization and influence on post harvest seafood quality, Marcel Dekker, New York, 271-315.

15. Kubo, I., & Kinst-Hori, I. (1998). Tyrosinase inhibitors from cumin. Agricultural Food Chemistry, 46, 5338-5341.

16. Kumar, A., Mishra, R., Singh, V.D., Mazumder, A., Mazumder, R., & Kumar, A. (2022). Wound healing activity of punicalin and punicalagin isolated from punica granatum L. Rasayan. J. Chem., 15. https://doi.org/10.31788/RJC.2022.1516639

17. Li, Y., Guo, C., Yang, J., Wei, J., Xu, J., & Cheng, S. (2006). Evaluation of antioxidant properties of pomegranate peel extract in comparison with pomegranate pulp extract. Food Chemistry, 96, 254-260.

18. Lopez-Caballero, M.E., Martinez-Alvarez, O., Gomez-Guillen, M.D.C., & Montero, P. (2007). Quality of thawed deepwater pink shrimp (Parapenaeus longirostris) treated with melanosis-inhibiting formulations during chilled storage. Food Science and Technology, 42, 1029-1038.

19. Lu, G., Wang, X., Cheng, M., Wang, S., & Ma, K. (2023). The multifaceted mechanisms of ellagic acid in the treatment of tumors: state-of-the-art. Biomed. Pharmacother., 165. https://doi.org/10.1016/j.biopha.2023.115132

20. Matinfar, A. (2010). Introduction of Litopenaeus vannamei to shrimp industry of Iran. Final report of research project. I. F.R.O, 42.

21. Peng, J., Zhao, X., Zhang, M., Li, J., Zhao, C., Wang, S., Wang, J., Shi, H., Zhou, P., & Wang, L. (2023). Punicalagin attenuates ventricular remodeling after acute myocardial infarction via regulating the NLRP3/caspase-1 pathway. Pharm. Biol., 61. https://doi.org/10.1080/13880209.2023.2224403

22. Zhang, L., Chinnathambi, A., Alharbi, S.A., Veeraraghavan, V.P., Mohan, S.K., & Zhang, G. (2020). Punicalagin promotes the apoptosis in human cervical cancer (ME-180) cells through mitochondrial pathway and by inhibiting the NF-kB signaling pathway. Saudi. J. Biol. Sci., 27. https://doi.org/10.1016/j.sjbs.2020.02.015