





Editorial

Editorial for the Special Issue “Pharmacological Activities and Mechanisms of Action of Natural Products”

Shining Loo ^{1,*} , Antony Kam ^{2,*} , Chunyue Du ² and Simon Ming-Yuen Lee ^{3,4}

¹ Wisdom Lake Academy of Pharmacy, Xi’an Jiaotong-Liverpool University, Wuzhong No.111, Renai Road, Suzhou 215123, China

² Department of Biosciences and Bioinformatics, Xi’an Jiaotong-Liverpool University, Wuzhong No.111, Renai Road, Suzhou 215123, China; chunyue.du@xjtlu.edu.cn

³ State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China; simon-my.lee@polyu.edu.hk

⁴ Department of Food Science and Nutrient, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China

* Correspondence: shining.loo@xjtlu.edu.cn (S.L.); antony.kam@xjtlu.edu.cn (A.K.)

1. Introduction

Natural products have long fascinated scientists as a vast source of structurally diverse bioactive compounds, serving as templates for many contemporary pharmaceuticals. This Special Issue of *Current Issues in Molecular Biology*, titled “Pharmacological Activities and Mechanisms of Action of Natural Products”, features 16 original research articles and reviews exploring the pharmacological profiles of compounds from fungi, medicinal herbs, fruits, higher plants, and purified molecules.

These works employ rigorous mechanistic analyses and therapeutic assessments to show how natural products regulate essential biological processes, such as alleviating oxidative stress, suppressing inflammatory pathways, modulating immune responses, and restoring metabolic balance. This approach not only identifies new therapeutic targets but also accelerates translation from laboratory discoveries to clinical applications. In this editorial, we provide an integrated overview of all 16 contributions, organized thematically to illuminate the current state and future directions in natural product pharmacology.

2. Fungal Natural Product Pharmacology

Macrofungi are rich in structurally complex bioactives, especially polysaccharides and triterpenoids [1,2], which display robust antioxidant, immunomodulatory, and anti-neoplastic effects via mechanisms like reactive oxygen species (ROS) neutralization and apoptosis induction.

Three contributions in this Special Issue:

- Research on wild *Ganoderma lucidum* from high-altitude regions shows that extraction solvent polarity markedly affects bioactive profiles and pharmacological outcomes [3].
- Complementary studies reveal *G. lucidum* extracts’ anti-senescence effects, including reduced oxidative stress and cellular aging, with potential dermatological uses dependent on standardized extraction methods [4].
- A review of *Inonotus obliquus* (chaga mushroom) outlines its anti-inflammatory and antineoplastic mechanisms via Nrf2 and NF-κB pathway modulation. It advocates metabolic engineering for sustainable production, while addressing translational hurdles, and extends to triterpenoids and melanin fractions that boost follicular regeneration under environmental stress (**Contribution 1**).



Received: 25 August 2025

Accepted: 5 September 2025

Published: 11 September 2025

Citation: Loo, S.; Kam, A.; Du, C.; Lee, S.M.-Y. Editorial for the Special Issue “Pharmacological Activities and Mechanisms of Action of Natural Products”. *Curr. Issues Mol. Biol.* **2025**, *47*, 743. <https://doi.org/10.3390/cimb47090743>

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

3. Polyherbal Formulation Natural Product Pharmacology

Traditional polyherbal blends often yield synergistic effects surpassing those of isolated components [5–7], excelling in anti-inflammatory actions, wound healing, and metabolic regulation through cytokine modulation and enzymatic interventions.

One contribution in this Special Issue:

- A standardized formulation of five Korean medicinal herbs (HRMC5) boosts dermal cell viability, provides UV photoprotection, speeds wound healing, and eases menopausal symptoms, supporting its role in dermatological therapies [8].

4. Fruit- and Plant-Derived Natural Product Pharmacology

Fruits and plants offer accessible bioactives [9,10] with proven cardiovascular benefits, achieved through lipid regulation, oxidative stress reduction, and inflammation control, alongside emerging roles in regenerative medicine.

Four contributions in this Special Issue:

- Red watermelon (*Citrullus lanatus*) compounds exhibit atheroprotective effects by inhibiting macrophage lipid buildup and enhancing reverse cholesterol transport, endorsing dietary strategies for cardiovascular prevention [11].
- *Platyclusus orientalis* leaf extract promotes follicular regeneration via dermal papilla cell proliferation and canonical pathway activation, suggesting applications in hair loss prevention and growth promotion (**Contribution 2**).
- *Nelumbo nucifera* (lotus) leaf extracts alleviate inflammatory diarrhea in models by suppressing pro-inflammatory mediators and apoptosis through pathway inhibition, positioning them as natural anti-inflammatory agents (**Contribution 3**).
- *Litchi chinensis* (Lychee) pericarp extracts reduce hyperuricemia via xanthine oxidase inhibition and improved renal uric acid excretion, validating their use as functional nutraceuticals (**Contribution 4**).

5. Bioactive Molecule Natural Product Pharmacology

Purified natural product molecules enable the precise targeting of disease pathways, offering insights into their roles in inflammation, oxidative stress, metabolism, and cellular protection.

Eight contributions in this Special Issue:

- Compounds like quercetin modulates the phosphomonoesterase activity of protein tyrosine phosphatase nonreceptor type 22, a key immune regulator with implications for cancer and autoimmune therapies (**Contribution 5**).
- Curcumin from *Curcuma longa* attenuates denervation-induced muscle atrophy by regulating inflammatory mediators and calcium homeostasis, building on its established anti-inflammatory profile [12].
- Fraxin, a coumarin glucoside from *Fraxinus* species, curbs inflammatory responses and foam cell formation via targeted pathway inhibition, aiding in vascular pathology management [13].
- Abrin, a ribosome-inactivating protein from *Abrus precatorius*, exhibits paradoxical effects in inhibiting protein synthesis in certain cellular contexts while potentiating immune responses in others, suggesting potential applications in autoimmune disease modulation (**Contribution 6**).
- Notoginsenoside R1 from *Panax notoginseng* confers cardioprotection against ischemia-reperfusion injury through the preservation of mitochondrial integrity and ROS mitigation [14].

- Tauroursodeoxycholic acid (TUDCA), a naturally produced hydrophilic bile acid, protects retinal cells from oxidative damage through autophagy induction, with potential of being an age-related macular degeneration therapeutic (**Contribution 7**).
- 3-Deoxysappanchalcone, a chalcone derived from *Caesalpinia sappan*, mitigates fine particulate matter (PM_{2.5})-induced pulmonary injury through the preservation of endothelial barrier function and inflammatory suppression [15].
- Paclitaxel, a naturally occurring diterpenoid compound extracted from the bark of Pacific yew tree, induces endoplasmic reticulum stress in reproductive tissues, revealing fertility implications that necessitate protective co-therapeutic strategies (**Contribution 8**).

6. Concluding Perspectives and Future Directions

This Special Issue vividly illustrates the broad therapeutic promise of natural products from fungi, herbs, fruits, plants, and purified molecules. These agents adeptly target pathways underlying oxidative stress, inflammation, metabolism, and cancer, merging ethnopharmacological heritage with cutting-edge molecular insights. Key takeaways include the need for optimized extraction techniques, standardization, and quality control to ensure consistent efficacy.

Although preclinical data are encouraging, advancing to clinical stages requires robust trials, advanced analytics, and thorough safety assessments. Ultimately, natural products bridge ancient wisdom and modern innovation, offering fertile ground for novel drugs to tackle pressing health challenges [16–18].

Funding: This research was supported in part by Xi'an JiaoTong Liverpool University Research Development Fund (RDF-23-01-007 and RDF-23-01-008). S.L. and A.K. would also like to acknowledge the support of Jiangsu Province Higher Education Key Laboratory of Cell Therapy Nanoformulation, Suzhou Municipal Key Lab for Metabolic Syndrome Drug Research, Suzhou Municipal Key Lab of Biomedical Sciences and Translational Immunology, XJTLU Wisdom Lake Academy of Pharmacy-BEAVER Biomedical Joint Laboratory Fund (RDS10120220047), and the GenScript Life Science Research Grant Program.

Conflicts of Interest: The authors declare no conflicts of interest.

List of Contributions

1. Wang, Y.; Gu, J.; Wu, J.; Xu, Y.; Liu, Y.; Li, F.; Liu, Q.; Lu, K.; Liang, T.; Hao, J.; et al. Natural Products and Health Care Functions of *Inonotus obliquus*. *Curr. Issues Mol. Biol.* **2025**, *47*, 269.
2. Kim, J.; Joo, J.H.; Kim, J.; Rim, H.; Shin, J.Y.; Choi, Y.-H.; Min, K.; Lee, S.Y.; Jun, S.-H.; Kang, N.-G. *Platyclus orientalis* Leaf Extract Promotes Hair Growth via Non-Receptor Tyrosine Kinase ACK1 Activation. *Curr. Issues Mol. Biol.* **2024**, *46*, 11207–11219.
3. Zheng, Y.; Zheng, J.; Wang, J.; Li, J.; Liu, J.; Zheng, B.; Li, Q.; Huang, X.; Lin, Z. Network Pharmacology and In Vitro Experimental Validation Reveal the Anti-Inflammatory and Anti-Apoptotic Effects of Lotus Leaf Extract in Treating Inflammatory Diarrhea in Pigs. *Curr. Issues Mol. Biol.* **2025**, *47*, 314.
4. Guo, Z.; Zhang, L.; Liu, J.; Yang, Z. Lychee Peel Extract Ameliorates Hyperuricemia by Regulating Uric Acid Production and Excretion in Mice. *Curr. Issues Mol. Biol.* **2025**, *47*, 76.

5. Sulyman, A.O.; Yusuf, T.N.A.; Aribisala, J.O.; Ibrahim, K.S.; Ajani, E.O.; Ajiboye, A.T.; Sabiu, S.; Singh, K. Quercetin as a Modulator of PTPN22 Phosphomonoesterase Activity: A Biochemical and Computational Evaluation. *Curr. Issues Mol. Biol.* **2024**, *46*, 11156–11175.
6. Hernlem, B.; Rasooly, R. Abrin Toxin Paradoxically Increases Protein Synthesis in Stimulated CD4+ T-Cells While Decreasing Protein Synthesis in Kidney Cells. *Curr. Issues Mol. Biol.* **2024**, *46*, 13970–13978.
7. Zubieta, D.; Warden, C.; Bhattacharya, S.; Brantley, M.A. Tauroursodeoxycholic Acid Confers Protection Against Oxidative Stress via Autophagy Induction in Retinal Pigment Epithelial Cells. *Curr. Issues Mol. Biol.* **2025**, *47*, 224.
8. Karadeniz Saygılı, S.; Sahin, M.C.; Yukcu, F.; Sanli, S. Analysis of Endoplasmic Reticulum Stress Proteins in Spermatogenic Cells After Paclitaxel Administration. *Curr. Issues Mol. Biol.* **2025**, *47*, 620.

References

1. Lu, H.; Lou, H.; Hu, J.; Liu, Z.; Chen, Q. Macrofungi: A review of cultivation strategies, bioactivity, and application of mushrooms. *Compr. Rev. Food Sci. Food Saf.* **2020**, *19*, 2333–2356. [[CrossRef](#)] [[PubMed](#)]
2. Niego, A.G.; Rapior, S.; Thongklang, N.; Raspé, O.; Jaidee, W.; Lumyong, S.; Hyde, K.D. Macrofungi as a nutraceutical source: Promising bioactive compounds and market value. *J. Fungi* **2021**, *7*, 397. [[CrossRef](#)] [[PubMed](#)]
3. Thapa, I.; Pandey, A.; Tiwari, S.; Awal, S.C. Evaluation of Bioactive Compounds, Antioxidant Activity, and Anticancer Potential of Wild *Ganoderma lucidum* Extracts from High-Altitude Regions of Nepal. *Curr. Issues Mol. Biol.* **2025**, *47*, 624. [[CrossRef](#)] [[PubMed](#)]
4. Kühnel, H.; Seiler, M.; Feldhofer, B.; Ebrahimian, A.; Maurer, M. *Ganoderma lucidum* Extract Modulates Gene Expression Profiles Associated with Antioxidant Defense, Cytoprotection, and Senescence in Human Dermal Fibroblasts: Investigation of Quantitative Gene Expression by qPCR. *Curr. Issues Mol. Biol.* **2025**, *47*, 130. [[CrossRef](#)] [[PubMed](#)]
5. Karole, S.; Shrivastava, S.; Thomas, S.; Soni, B.; Khan, S.; Dubey, J.; Dubey, S.P.; Khan, N.; Jain, D.K. Polyherbal Formulation Concept for Synergic Action: A Review. *J. Drug Deliv. Ther.* **2019**, *9*, 453–466. [[CrossRef](#)]
6. Zhou, X.; Seto, S.W.; Chang, D.; Kiat, H.; Razmovski-Naumovski, V.; Chan, K.; Bensoussan, A. Synergistic effects of Chinese herbal medicine: A comprehensive review of methodology and current research. *Front. Pharmacol.* **2016**, *7*, 201. [[CrossRef](#)] [[PubMed](#)]
7. Aslam, M.S.; Ahmad, M.S.; Mamat, A.S.; Ahmad, M.Z.; Salam, F. An update review on polyherbal formulation: A global perspective. *Syst. Rev. Pharm.* **2016**, *7*, 35–41. [[CrossRef](#)]
8. Ha, R.; Cho, W.K.; Kim, E.; Jang, S.J.; Kim, J.-D.; Yi, C.-G.; Moh, S.H. Exploring the Benefits of Herbal Medicine Composite 5 (HRMC5) for Skin Health Enhancement. *Curr. Issues Mol. Biol.* **2024**, *46*, 12133–12151. [[CrossRef](#)] [[PubMed](#)]
9. Karasawa, M.M.G.; Mohan, C. Fruits as prospective reserves of bioactive compounds: A review. *Nat. Prod. Bioprospecting* **2018**, *8*, 335–346. [[CrossRef](#)] [[PubMed](#)]
10. Shashirekha, M.; Mallikarjuna, S.; Rajarathnam, S. Status of bioactive compounds in foods, with focus on fruits and vegetables. *Crit. Rev. Food Sci. Nutr.* **2015**, *55*, 1324–1339. [[CrossRef](#)] [[PubMed](#)]
11. Bahrudin, M.; Al Fauzi, A.; Sugianto, P. Effectiveness of Red Watermelon in Preventing Atherosclerosis Through the Role of Lipids, PCSK9, LOX-1, CD36, and ABCA1 in Wistar Rats. *Curr. Issues Mol. Biol.* **2025**, *47*, 433. [[CrossRef](#)] [[PubMed](#)]
12. Appell, C.; Jiwan, N.C.; Shen, C.-L.; Luk, H.-Y. Curcumin Mitigates Muscle Atrophy Potentially by Attenuating Calcium Signaling and Inflammation in a Spinal Nerve Ligation Model. *Curr. Issues Mol. Biol.* **2024**, *46*, 12497–12511. [[CrossRef](#)] [[PubMed](#)]
13. Wang, Y.; Wei, B.; Leng, M.; He, J.; Zhao, Y.; Xia, H.; Luo, H.; Bai, X. Fraxin Alleviates Atherosclerosis by Inhibiting Oxidative Stress and Inflammatory Responses via the TLR4/PI3K/Akt Pathway. *Curr. Issues Mol. Biol.* **2025**, *47*, 308. [[CrossRef](#)] [[PubMed](#)]
14. Xu, Y.; Wang, P.; Hu, T.; Ning, K.; Bao, Y. Notoginsenoside R1 Attenuates H/R Injury in H9c2 Cells by Maintaining Mitochondrial Homeostasis. *Curr. Issues Mol. Biol.* **2025**, *47*, 44. [[CrossRef](#)] [[PubMed](#)]
15. Ryu, C.-W.; Lee, J.; Han, G.; Lee, J.-Y.; Bae, J.-S. Inhibitory Effects of 3-Deoxysappanchalcone on Particulate-Matter-Induced Pulmonary Injury. *Curr. Issues Mol. Biol.* **2025**, *47*, 608. [[CrossRef](#)] [[PubMed](#)]
16. Shrivastava, R.; Modi, G.; Satpathy, P.S.; Bandyopadhyay, S.; Kumar, Y.; Yadav, I. Natural Products Revolutionizing and Innovative Drug Discovery and Development Strategies: Healthcare Challenges and Future Perspectives. *J. Appl. Bioanal.* **2024**, *10*, 20–38.

17. Balkrishna, A.; Sharma, N.; Srivastava, D.; Kukreti, A.; Srivastava, S.; Arya, V. Exploring the safety, efficacy, and bioactivity of herbal medicines: Bridging traditional wisdom and modern science in healthcare. *Future Integr. Med.* **2024**, *3*, 35–49. [[CrossRef](#)]
18. Thomford, N.E.; Senthebane, D.A.; Rowe, A.; Munro, D.; Seele, P.; Maroyi, A.; Dzobo, K. Natural products for drug discovery in the 21st century: Innovations for novel drug discovery. *Int. J. Mol. Sci.* **2018**, *19*, 1578. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.