

Editorial

Synthetic and Natural Drugs: Converging Frontiers in Drug Discovery, Pharmaceutical Innovation, and Translational Medicine

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1. Introduction

The remarkable progress achieved in pharmaceutical sciences over the past several decades has transformed our understanding of disease biology and significantly expanded the therapeutic options available for numerous human disorders. However, despite these advances, the translation of promising laboratory discoveries into clinically effective medicines remains an exceptionally challenging process [1–3]. The high attrition rate of drug candidates, increasing complexity of multifactorial diseases, emergence of antimicrobial resistance, and growing demand for personalized therapies all underscore the need for innovative and interdisciplinary approaches to drug discovery and development.

Historically, synthetic chemistry and natural product research have often been viewed as distinct avenues of therapeutic discovery. Today, however, these disciplines are increasingly recognized as complementary components of a unified drug development paradigm. Natural products continue to provide unparalleled structural diversity [4,5] and biological inspiration, while synthetic chemistry enables precise molecular optimization, scalable manufacturing, and rational target engagement. Equally importantly, advances in pharmaceutical engineering, biomaterials science, computational biology, and translational medicine are redefining how therapeutic molecules are discovered, optimized, delivered, and ultimately translated into clinical practice.

The Special Issue “Synthetic and Natural Drugs: Pharmacological Activity, Biochemical Properties, and Applications” was conceived with this multidisciplinary vision in mind. Although the seven contributions included in this collection span diverse therapeutic areas and experimental approaches, they collectively illustrate four scientific frontiers that are shaping the future of pharmaceutical research: (i) Discovery of bioactive molecules, (ii) Advancing pharmaceutical formulation, (iii) Biomaterials and localized therapeutics, and (iv) Future perspectives.



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2. Discovery of Bioactive Molecules

The continued search for biologically active molecules remains the foundation of pharmaceutical innovation [5]. While advances in synthetic chemistry have accelerated rational drug design, nature continues to provide an extraordinary source of structurally diverse compounds that have evolved to interact with biological systems in highly specific ways. Consequently, modern drug discovery increasingly combines natural product exploration with mechanistic pharmacology to identify novel therapeutic opportunities.

Several contributions in this Special Issue exemplify this direction. The investigation comparing puerarin with the clinically established local anesthetic lidocaine demonstrates how naturally occurring compounds may provide alternative strategies for modulating neuronal excitability associated with orofacial pain [Contribution 1]. Rather than merely identifying biological activity, this work advances a mechanistic understanding of pain signaling pathways, an essential step toward developing safer non-opioid analgesics.

Similarly, the study investigating aqueous extracts from the cyanobacterium *Chroococcus* sp. R-10 highlights the enormous potential of microbial biodiversity as a reservoir of bioactive molecules [Contribution 2] with antioxidant, antiproliferative, and proapoptotic properties. Such investigations continue to expand the repertoire of natural compounds available for future anticancer drug development while emphasizing the importance of identifying their active constituents and molecular targets.

Complementing these original investigations, the review article on lesser-known sodium-glucose cotransporter (SGLT) isoform inhibitors illustrates another important dimension of therapeutic discovery: identifying new biological targets rather than simply discovering new molecules. The remarkable success of SGLT2 inhibitors has transformed the treatment of diabetes and cardiovascular disease, yet growing evidence suggests that additional transporter isoforms may represent promising therapeutic targets [Contribution 3] across oncology, inflammation, neurodegeneration, and metabolic disorders. Together, these studies demonstrate that innovation in drug discovery is driven equally by discovering new compounds and by expanding our understanding of disease biology.

3. Advancing Pharmaceutical Formulation

The identification of a biologically active compound represents only the first step in drug development. Numerous promising molecules ultimately fail because of inadequate pharmaceutical properties, including poor solubility, instability, limited absorption, or unfavorable pharmacokinetics. Consequently, pharmaceutical formulation has evolved from a supporting discipline into a central driver of therapeutic innovation [6].

The application of hot-melt extrusion technology to improve the pharmaceutical performance of lycopene illustrates this transformation. Lycopene has long attracted scientific interest because of its antioxidant and anti-inflammatory properties, yet its poor aqueous solubility has limited broader therapeutic application. By enhancing its pharmaceutical characteristics through formulation engineering, this work demonstrates how existing natural compounds may acquire renewed clinical potential [Contribution 4] without altering their chemical identity.

A similar philosophy underlies the development of the chitosan hydrochloride–biosurfactant–grape seed oil nanoemulsion designed to combat dental biofilms. Rather than relying upon a single active ingredient, this multifunctional formulation integrates naturally derived biomaterials into a nanoscale delivery platform capable of simultaneously improving antimicrobial activity, disrupting biofilms, and maintaining acceptable biocompatibility. Such studies illustrate the increasing importance of formulation science as an enabling technology capable of enhancing efficacy while minimizing toxicity [Contribution 5].

Collectively, these investigations reinforce an important paradigm in contemporary pharmaceutical research: therapeutic success increasingly depends not only on discovering better molecules but also on developing better medicines.

4. Biomaterials and Localized Therapeutics

An equally significant trend emerging from modern pharmaceutical research is the convergence of drug delivery with biomaterials engineering. Advances in additive man-

ufacturing, biodegradable polymers, and implantable medical devices have enabled the development of therapeutic systems capable of providing localized drug release while simultaneously restoring tissue function [7].

This frontier is represented by the two complementary investigations utilizing melt-electrowritten polycaprolactone meshes for pelvic organ prolapse repair. One study demonstrates that incorporation of azithromycin coatings can provide localized antimicrobial protection while preserving favorable mechanical performance [Contribution 6]. The second illustrates how antistatic modification of biodegradable meshes improves fabrication quality and device performance [Contribution 7]. Although differing in their engineering objectives, both studies reflect the broader movement toward multifunctional therapeutic devices in which structural support, infection control, and tissue regeneration are integrated within a single platform.

These contributions emphasize that future pharmaceutical innovation will increasingly occur at the interface of chemistry, materials science, engineering, and regenerative medicine, where drugs and medical devices become components of unified therapeutic systems rather than independent technologies.

5. Future Perspectives

Collectively, the studies presented in this Special Issue illustrate the remarkable evolution of pharmaceutical sciences from molecule-centered research toward systems-oriented therapeutic development. Future advances will likely depend upon the integration of several emerging technologies.

Artificial intelligence and machine learning are already accelerating target identification, lead optimization, and the prediction of pharmacokinetic and toxicological properties [8,9]. Multi-omics technologies, including genomics, transcriptomics, proteomics, metabolomics, and spatial biology, are providing unprecedented insight into disease mechanisms and patient heterogeneity. Precision medicine approaches promise increasingly individualized therapies tailored to molecular biomarkers rather than disease classification alone [10].

Equally important will be continued advances in nanomedicine, controlled-release systems, biodegradable biomaterials, and stimuli-responsive drug delivery technologies capable of maximizing therapeutic efficacy while minimizing systemic toxicity. Sustainable pharmaceutical manufacturing and environmentally responsible utilization of natural resources will also become increasingly important as the global demand for medicines continues to grow.

Perhaps the most important lesson emerging from this Special Issue is that the future of drug discovery will not be defined by choosing between synthetic and natural products. Instead, meaningful therapeutic innovation will arise from their convergence. Natural compounds provide unique molecular scaffolds and biological inspiration; synthetic chemistry enables optimization and scalability; pharmaceutical engineering improves clinical performance; biomaterials facilitate targeted delivery; and computational sciences accelerate every stage of development [5,8]. The integration of these disciplines represents the future of pharmaceutical science.

The articles collected in this Special Issue collectively demonstrate that innovation is no longer measured solely by the discovery of new molecules, but by our ability to transform biological insight into clinically meaningful therapeutic solutions. We hope that this collection encourages continued interdisciplinary collaboration, stimulates new scientific questions, and inspires future investigations that bridge the traditional boundaries separating chemistry, biology, engineering, and medicine.

As Guest Editors, we extend our sincere gratitude to all authors for sharing their excellent work, to the reviewers for their thoughtful and constructive evaluations, and to the editorial team of *Applied Sciences* for their outstanding support throughout the publication process. It has been a privilege to oversee this Special Issue, and we hope that the scientific advances presented herein will contribute to future discoveries and ultimately improve human health through continued innovation in synthetic and natural drug research.

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List of Contributions

1. Hirano, R.; Chida, R.; Utugi, S.; Takeda, M. Comparative Evaluation of Puerarin and Lidocaine on the Excitability of Trigeminal Wide-Dynamic-Range Neurons: Potential for Orofacial Pain Management. *Appl. Sci.* **2026**, *16*, 1607. <https://doi.org/10.3390/app16031607>.
2. Sulikovska, I.; Toshkova-Yotova, T.; Tsvetanova, E.; Djeliova, V.; Lozanova, V.; Vasileva, A.; Ivanov, I.; Toshkova, R.; Georgieva, A. Assessment of Antioxidant, Antiproliferative and Proapoptotic Potential of Aqueous Extracts of *Chroococcus* sp. R-10. *Appl. Sci.* **2025**, *15*, 10628. <https://doi.org/10.3390/app151910628>.
3. Berecka-Rycerz, A.; Gumieniczek, A.; Skroban, J.; Wicha-Komsta, K. Beyond SGLT2: Exploring the Therapeutic Potential of Lesser-Known SGLT Isoform Inhibitors. *Appl. Sci.* **2025**, *15*, 11603. <https://doi.org/10.3390/app152111603>.
4. Kulawik, A.; Kulawik, M.; Rosiak, N.; Lu, W.; Kryszak, A.; Cielecka-Piontek, J.; Zalewski, P. Improving the Pharmaceutical Potential of Lycopene Using Hot-Melt Extrusion. *Appl. Sci.* **2025**, *15*, 12311. <https://doi.org/10.3390/app152212311>.
5. Stamford, T.C.M.; Sa, A.V.P.; Berger, L.R.R.; De Freitas Pontes Macedo, I.T.; Xavier-Júnior, F.H.; Rufino, R.D.; Sarubbo, L.A.; Diaz De Rienzo, M.A. A Novel Chitosan Hydrochloride–Biosurfactant–Grape Seed Oil Nanoemulsion to Control Dental Carie: Antimicrobial, Antibiofilm Activity and Irritation Potential. *Appl. Sci.* **2025**, *15*, 11773. <https://doi.org/10.3390/app152111773>.
6. Martins, J.P.; Sousa, A.S.; Costa De Oliveira, S.; Fernandes, A.A.; Silva, E. Mechanical Characterization and Azithromycin Coating of Melt Electrowritten Polycaprolactone Mesh Implants for Prolapse Repair. *Appl. Sci.* **2025**, *15*, 9436. <https://doi.org/10.3390/app15179436>.
7. Cruz, D.; Vaz, F.; Antoniadi, E.; Silva, A.T.; Martins, J.; Pinheiro, F.; Ferreira, N.M.; Bebiano, L.B.; Pereira, R.F.; Fernandes, A.; et al. Antistatic Melt-Electrowritten Biodegradable Mesh Implants for Enhanced Pelvic Organ Prolapse Repair. *Appl. Sci.* **2025**, *15*, 7763. <https://doi.org/10.3390/app15147763>.

References

1. Waring, M.J.; Arrowsmith, J.; Leach, A.R.; Leeson, P.D.; Mandrell, S.; Owen, R.M.; Pairaudeau, G.; Pennie, W.D.; Pickett, S.D.; Wang, J.; et al. An Analysis of the Attrition of Drug Candidates from Four Major Pharmaceutical Companies. *Nat. Rev. Drug Discov.* **2015**, *14*, 475–486. [[CrossRef](#)] [[PubMed](#)]
2. Rennane, S.; Baker, L.; Mulcahy, A. Estimating the Cost of Industry Investment in Drug Research and Development: A Review of Methods and Results. *Inq. J. Health Care Organ. Provis. Financ.* **2021**, *58*, 00469580211059731. [[CrossRef](#)] [[PubMed](#)]
3. Schlander, M.; Hernandez-Villafuerte, K.; Cheng, C.-Y.; Mestre-Ferrandiz, J.; Baumann, M. How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *Pharmacoeconomics* **2021**, *39*, 1243–1269. [[CrossRef](#)] [[PubMed](#)]
4. Newman, D.J.; Cragg, G.M. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. *J. Nat. Prod.* **2020**, *83*, 770–803. [[CrossRef](#)] [[PubMed](#)]
5. Atanasov, A.G.; Zotchev, S.B.; Dirsch, V.M.; The International Natural Product Sciences Taskforce; Orhan, I.E.; Banach, M.; Rollinger, J.M.; Barreca, D.; Weckwerth, W.; Bauer, R.; et al. Natural Products in Drug Discovery: Advances and Opportunities. *Nat. Rev. Drug Discov.* **2021**, *20*, 200–216. [[CrossRef](#)] [[PubMed](#)]

6. Repka, M.A.; Bandari, S.; Kallakunta, V.R.; Vo, A.Q.; McFall, H.; Pimparade, M.B.; Bhagurkar, A.M. Melt Extrusion with Poorly Soluble Drugs—An Integrated Review. *Int. J. Pharm.* **2018**, *535*, 68–85. [[CrossRef](#)] [[PubMed](#)]
7. Li, C.; Guo, C.; Fitzpatrick, V.; Ibrahim, A.; Zwierstra, M.J.; Hanna, P.; Lechtig, A.; Nazarian, A.; Lin, S.J.; Kaplan, D.L. Design of Biodegradable, Implantable Devices towards Clinical Translation. *Nat. Rev. Mater.* **2019**, *5*, 61–81. [[CrossRef](#)]
8. Vamathevan, J.; Clark, D.; Czodrowski, P.; Dunham, I.; Ferran, E.; Lee, G.; Li, B.; Madabhushi, A.; Shah, P.; Spitzer, M.; et al. Applications of Machine Learning in Drug Discovery and Development. *Nat. Rev. Drug Discov.* **2019**, *18*, 463–477. [[CrossRef](#)] [[PubMed](#)]
9. Paul, D.; Sanap, G.; Shenoy, S.; Kalyane, D.; Kalia, K.; Tekade, R.K. Artificial Intelligence in Drug Discovery and Development. *Drug Discov. Today* **2021**, *26*, 80–93. [[CrossRef](#)] [[PubMed](#)]
10. Denny, J.C.; Collins, F.S. Precision Medicine in 2030—Seven Ways to Transform Healthcare. *Cell* **2021**, *184*, 1415–1419. [[CrossRef](#)] [[PubMed](#)]

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