

Natural Compounds and Green Extraction: A Sustainable Approach for Management of Peptic Ulcer

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Abstract

Peptic ulcers have emerged as one of the leading world health problems with regard to the number of people suffering from it and the consequent economic and clinical load. Current therapy is usually on synthetic drugs, which despite their proven efficacy, present notable drawbacks, including side effects and antibiotic resistance. The present review brings emphasis to the considerable potential inherent in natural compounds like flavonoids, alkaloids, and terpenoids as safe, multi-target alternatives. Green chemistry is held to be really transforming the discovery and development of anti-ulcer agents. Supercritical fluid and microwave-assisted extraction methods constitute techniques that have gone green in providing sustainable and novel ways of isolating bioactives. Their successful alignment towards environmental goals and compounding efficacy preservation has made them really appealing. In addition, the application of computer methods, such as QSAR modeling and docking studies, optimizes bioactivity in the virtue of green chemistry. The integration of these advanced approaches marks a transformative change toward sustainable and effective therapies for managing peptic ulcers, addressing both therapeutic and ecological imperatives.

Keywords:

Peptic ulcers, green chemistry, sustainable drug development, eco-friendly extraction, phytochemicals.

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Overview of ulcers as a global health problem

Ulcers, particularly peptic ulcers, represent a significant global health issue affecting millions of individuals each year. These lesions occur in the lining of the stomach or duodenum, primarily due to an imbalance between protective factors, such as mucus and bicarbonate secretion, and damaging agents, such as gastric acid and pepsin [1]. The prevalence of ulcers is influenced by several factors, including infection with *Helicobacter pylori*, chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), excessive alcohol consumption, and smoking. Beyond physical discomfort, ulcers impose a substantial economic burden on healthcare systems worldwide, stemming from direct medical expenses, absenteeism from work, and decreased quality of life. If left untreated, ulcers can lead to severe complications such as bleeding, perforation, and even gastric cancer, emphasizing the need for effective and accessible treatment strategies [2, 3].

Challenges of current synthetic anti-ulcer drugs including side effects and resistance

Synthetic drugs, such as proton pump inhibitors (PPIs), H₂-receptor antagonists, and antacids, have been the mainstay of ulcer treatment for decades. While these medications are effective in managing symptoms and promoting healing, they are not without significant drawbacks. Long-term use of PPIs, for instance, has been associated with adverse effects, including nutrient malabsorption (e.g., vitamin B12 and magnesium), increased susceptibility to infections, and potential kidney damage. Moreover, reliance on antibiotics to eradicate *H. pylori* has led to the emergence of antibiotic-resistant strains, complicating treatment regimens and reducing success rates. These limitations highlight the need for alternative approaches that not only address the root causes of ulcers but also minimize adverse effects and reduce the likelihood of resistance [3].

Importance of natural compounds in respect to these challenges

Natural compounds derived from plants, marine organisms, and other biological sources offer a promising solution to the limitations of synthetic drugs. Many of these compounds possess inherent anti-ulcer properties, such as reducing gastric acid secretion, enhancing mucosal protection, and exerting antioxidant effects. [4] For example, flavonoids, alkaloids, and terpenoids have shown significant potential in preclinical studies as effective and safer alternatives to conventional therapies. Moreover, natural compounds often exhibit multi-target mechanisms of action, allowing them to address various aspects of ulcer pathophysiology simultaneously. The biocompatibility and lower toxicity profiles of these compounds make them particularly attractive candidates for developing sustainable and patient-friendly treatments [5].

The role of green chemistry in sustainable drug discovery

Green chemistry plays a pivotal role in the sustainable discovery and development of anti-ulcer agents from natural sources. This scientific discipline emphasizes the design of chemical processes and products that minimize environmental impact and reduce the use of hazardous substances. By adopting green chemistry principles, researchers can implement eco-friendly extraction techniques, such as supercritical fluid extraction and microwave-assisted extraction, to isolate bioactive compounds efficiently. [6] Additionally, green chemistry promotes the use of renewable feedstocks and biodegradable solvents, ensuring that drug development aligns with environmental and economic sustainability. The integration of green chemistry in natural product research not only advances the discovery of novel anti-ulcer agents but also addresses the broader goal of fostering a sustainable pharmaceutical industry [7].

Together, these factors underscore the critical need to explore and leverage green chemistry approaches in the pursuit of safer, more effective, and environmentally responsible anti-ulcer therapies [8].

Application of green chemistry principles in developing natural compounds

Green chemistry, a transformative approach to chemical research and industrial practices, focuses on reducing environmental harm while maintaining or improving the efficiency and safety of chemical processes. This philosophy is particularly relevant in the development of natural compounds for medicinal purposes, including anti-ulcer agents. One key principle of green chemistry is the use of renewable feedstocks, which encourages sourcing materials from sustainable and regenerative biological resources, such as plants or marine organisms. Unlike synthetic precursors derived from non-renewable petrochemicals, renewable feedstocks reduce the carbon footprint of drug development and ensure a consistent supply of raw materials [9].

Another critical principle is the reduction or elimination of hazardous substances during the extraction, synthesis, and processing stages. By avoiding toxic solvents, reagents, and by-products, researchers can enhance the safety of both the manufacturing process and the resulting pharmaceuticals. For instance, green solvents like ethanol, water, and supercritical CO₂ offer safer alternatives to conventional organic solvents, minimizing exposure risks and environmental contamination. The implementation of these principles not only ensures compliance with stringent regulatory standards but also aligns drug development with global sustainability goals [10].

Examples of green synthesis and extraction techniques

Modern green chemistry has revolutionized the extraction and synthesis of natural compounds through innovative techniques that maximize efficiency while minimizing environmental impact. Microwave-assisted extraction (MAE) is one such method, utilizing microwave energy to rapidly heat plant materials and solvents. This technique enhances the release of bioactive compounds by breaking down cell walls and improving solvent penetration. Compared to traditional extraction methods, MAE significantly reduces processing time, energy consumption, and solvent use, making it a highly sustainable option for isolating anti-ulcer agents from natural sources [11].

Another groundbreaking method is supercritical fluid extraction (SFE), which employs supercritical CO₂ as a solvent. In its supercritical state, CO₂ exhibits gas-like diffusion properties and liquid-like solvating power, enabling the efficient extraction of bioactive compounds without the need for toxic organic solvents. SFE is particularly advantageous for its ability to operate at relatively low temperatures, preserving the stability and bioactivity of heat-sensitive natural compounds. Additionally, the non-toxic and recyclable nature of CO₂ makes this technique environmentally friendly and cost-effective [12].

Other green techniques, such as ultrasound-assisted extraction (UAE) and pressurized liquid extraction (PLE), further exemplify the application of green chemistry in natural product research. These methods leverage advanced technologies to enhance yield, purity, and efficiency while reducing waste and energy input. By integrating these sustainable techniques into the drug discovery pipeline, researchers can accelerate the development of natural anti-ulcer compounds while adhering to the principles of green chemistry [13].

Classes of natural compounds with anti-ulcer effects

Natural compounds have garnered significant attention as potential anti-ulcer agents due to their bioactive properties and relative safety profiles. Among these, flavonoids, alkaloids, and terpenoids are the most extensively studied classes, each demonstrating unique mechanisms of action in preventing and healing ulcers [14].

Flavonoids are polyphenolic compounds abundantly found in fruits, vegetables, and medicinal plants. These compounds exhibit potent antioxidant activity, neutralizing free radicals that contribute to oxidative stress and gastric mucosal damage. Flavonoids such as quercetin, rutin, and catechin have shown remarkable efficacy in reducing gastric acid secretion, promoting mucus production, and enhancing mucosal blood flow. These properties collectively contribute to the repair and maintenance of the gastric lining, making flavonoids effective in both ulcer prevention and treatment [15].

Alkaloids, a diverse group of nitrogen-containing compounds, are another important class of natural anti-ulcer agents. Found in various plants like *Papaver* and *Rauwolfia*, alkaloids such as berberine, atropine, and piperine possess significant gastroprotective properties. They act by modulating gastric acid secretion, inhibiting the growth of *Helicobacter pylori*, and exerting anti-inflammatory effects. Berberine, in particular, has been shown to strengthen the gastric mucosal barrier while reducing oxidative and inflammatory damage, highlighting its multifaceted role in ulcer management [16].

Terpenoids, derived from the isoprene unit, represent one of the largest classes of natural compounds with anti-ulcer activity. Monoterpenes like menthol and sesquiterpenes like β -caryophyllene have demonstrated their ability to reduce gastric acid secretion and enhance mucosal protection. Additionally, triterpenoids, such as ursolic acid and oleanolic acid, exhibit anti-inflammatory, antioxidant, and anti-*H. pylori* activities, further supporting their therapeutic potential in managing gastric ulcers [17].

Mechanisms of action for anti-ulcer natural compounds

The effectiveness of these natural compounds lies in their ability to target multiple pathways involved in ulcer formation and healing. One of the primary mechanisms is their antioxidant activity, which mitigates oxidative stress caused by reactive oxygen species (ROS). By scavenging free radicals, compounds like flavonoids and terpenoids prevent lipid peroxidation and cellular damage in the gastric mucosa.

Another critical mechanism is mucosal protection. Many natural compounds stimulate the secretion of mucus and bicarbonate, creating a protective barrier against gastric acid and pepsin. This barrier helps shield the epithelium from corrosive substances and supports the regeneration of damaged tissue. Flavonoids, for instance, enhance mucus production and improve microcirculation, which are vital for maintaining mucosal integrity [18].

Anti-inflammatory effects also play a pivotal role, as inflammation exacerbates ulcer formation. Natural compounds like alkaloids and triterpenoids reduce the levels of pro-inflammatory cytokines, such as TNF- α and IL-6, thereby alleviating gastric inflammation and promoting healing, Figure 1.

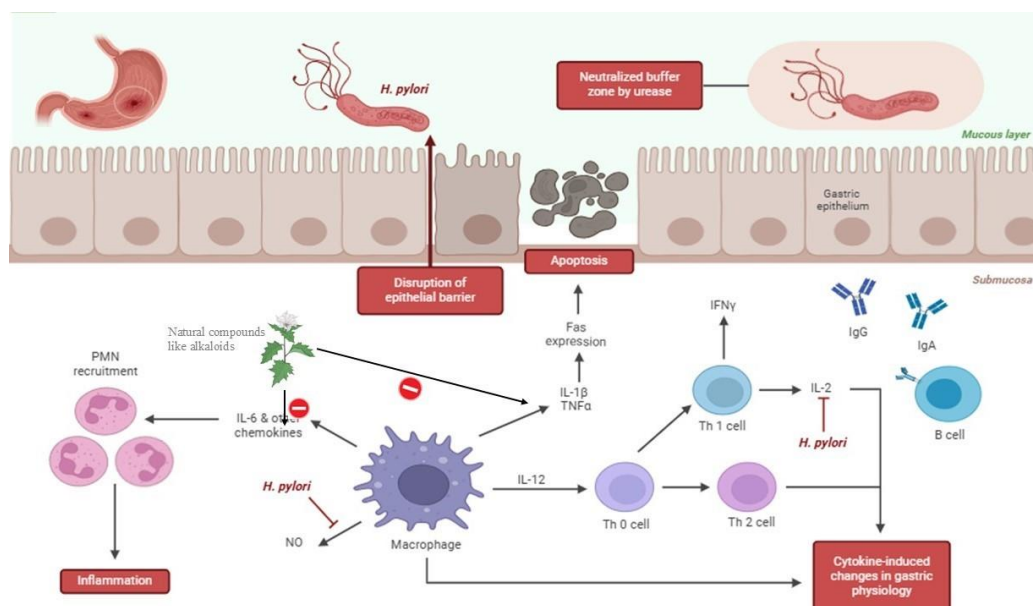


Figure 1: Mechanisms of action of natural compounds for treatment of peptic ulcer induced by *H. pylori*

Furthermore, some natural compounds exhibit anti-*Helicobacter pylori* activity, directly targeting the bacterium responsible for a significant proportion of peptic ulcers. This includes inhibition of bacterial adhesion, disruption of biofilm formation, and interference with bacterial virulence factors.

Lastly, natural compounds may regulate gastric acid secretion by modulating the activity of proton pumps or histamine receptors. This reduces the corrosive effects of gastric acid on the stomach lining, providing relief from ulcer symptoms and fostering tissue repair.

Together, the diverse classes of natural compounds and their multifaceted mechanisms of action present a promising avenue for developing safer, more effective therapies for ulcers. Their ability to act on multiple targets makes them particularly advantageous in addressing the complex pathophysiology of ulcer diseases [19].

Green extraction methods for bioactive compounds isolation from plants

Green extraction methods have revolutionized the process of isolating bioactive compounds from plants by incorporating principles of sustainability, efficiency, and environmental safety. These methods aim to minimize the use of harmful solvents, reduce energy consumption, and maximize the yield of bioactive compounds while preserving their integrity. Techniques such as supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), and ultrasound-assisted extraction (UAE) are among the most widely used green extraction methods.

Supercritical fluid extraction (SFE) utilizes supercritical CO₂ as a solvent, which combines the properties of a gas and a liquid to efficiently dissolve and extract bioactive compounds. This method is particularly suitable for heat-sensitive compounds due to its operation at moderate temperatures. Microwave-assisted extraction (MAE) uses microwave energy to heat plant material and solvents uniformly, breaking down plant cell walls and facilitating the release of bioactives in a fraction of the time required by conventional methods. Similarly, ultrasound-assisted extraction (UAE) employs ultrasonic waves to create microbubbles and cavitation in the solvent, disrupting plant cell walls and enhancing the diffusion of bioactive compounds into the solvent [20].

These techniques, collectively referred to as green extraction methods, prioritize environmental compatibility and resource efficiency, offering a sustainable pathway for natural product discovery.

Eco-friendly solvents and techniques versus traditional methods

Green extraction methods provide several advantages over traditional solvent-based extraction techniques. One of the primary benefits is the reduction in toxic solvent usage, which enhances worker safety and minimizes environmental pollution. For example, SFE employs CO₂, which is non-toxic, inert, and recyclable, in contrast to organic solvents that are often volatile and hazardous. Similarly, MAE and UAE allow the use of water or ethanol as solvents, further reducing the reliance on harmful chemicals [21].

These methods also offer significant improvements in energy efficiency and time savings. Traditional extraction methods often require long processing times and high temperatures, which can degrade sensitive bioactive compounds. Green techniques like MAE and UAE operate at lower temperatures and significantly shorter durations, preserving the bioactivity and structural integrity of extracted compounds. Additionally, these methods improve the yield and purity of target compounds by optimizing extraction conditions, ensuring that the process is both economical and effective [22].

Furthermore, the scalability and adaptability of green extraction methods make them suitable for industrial applications. Techniques like SFE can be precisely controlled to target specific compounds, reducing waste and enhancing selectivity. These advantages collectively underscore the value of green extraction in sustainable natural product research and pharmaceutical development [23].

Case studies of green extraction for anti-ulcer agents

Several case studies highlight the successful application of green extraction methods in isolating anti-ulcer compounds from plant sources. For instance, the extraction of flavonoids from *Glycyrrhiza glabra* (licorice) using supercritical CO₂ has demonstrated high efficiency and purity. Flavonoids like liquiritigenin and isoliquiritigenin, known for their gastroprotective and anti-inflammatory properties, were effectively isolated without the use of toxic solvents, preserving their pharmacological activity [24].

Another example is the use of microwave-assisted extraction to isolate polyphenols from *Punica granatum* (pomegranate) peels. Polyphenols such as punicalagin and ellagic acid exhibit strong antioxidant and mucosal protective effects, making them potent candidates for anti-ulcer therapy. MAE significantly reduced extraction time while maximizing the yield of these bioactives, showcasing the method's efficiency and sustainability [25].

Ultrasound-assisted extraction has also been employed to extract terpenoids from *Artemisia* species, which are known for their anti-ulcer and antimicrobial activities. UAE enhanced the extraction of artemisinin and related compounds with minimal solvent use, aligning with green chemistry principles [26].

These case studies exemplify how green extraction methods not only improve the efficiency and safety of bioactive compound isolation but also contribute to the discovery of novel anti-ulcer agents. The integration of such methods in pharmaceutical research ensures the development of environmentally friendly and clinically effective therapies [27].

High-throughput screen methods for identifying anti-ulcer compounds from natural sources

High-throughput screening (HTS) has become a powerful tool in the discovery of novel anti-ulcer compounds from natural sources, enabling the rapid and efficient evaluation of large numbers of compounds for their biological activity. HTS involves the use of automated systems to test a wide range of natural extracts or purified compounds against specific biological targets, such as gastric acid secretion, *Helicobacter pylori* inhibition, or mucosal protection. The advantages of HTS include its ability to process thousands of compounds simultaneously, saving significant time and resources in the early stages of drug discovery [28].

One approach to HTS in anti-ulcer research is the use of cell-based assays to assess the protective effects of natural compounds on gastric epithelial cells or their ability to modulate gastric acid secretion. These assays can evaluate the cytotoxicity, antioxidative, anti-inflammatory, and mucosal protective activities of compounds, providing a comprehensive overview of their potential efficacy. Enzyme-linked immunosorbent assays (ELISA) and fluorescence-based assays are commonly used for detecting specific biomarkers, such as cytokines or oxidative stress markers, which are relevant in ulcer pathophysiology [29].

Another approach is receptor-based assays, where natural compounds are screened for their ability to interact with specific receptors involved in ulcer development, such as the histamine H₂ receptor or the proton pump. HTS can also utilize microfluidic systems to simulate gastrointestinal conditions, providing more physiologically relevant data about the compounds' anti-ulcer properties. Overall, HTS techniques allow researchers to quickly identify promising natural anti-ulcer candidates, which can then be subjected to further validation and optimization [30].

Computational approaches to optimize bioactivity with green chemistry principles

Computational approaches, including quantitative structure-activity relationship (QSAR) modeling and docking studies, play a vital role in optimizing the bioactivity of natural compounds while adhering to green chemistry principles. These methods enable researchers to predict the biological activity and potential toxicity of compounds before conducting time-consuming and resource-intensive laboratory experiments. This not only accelerates the drug discovery process but also ensures that only the most promising candidates are selected for further investigation, reducing the environmental and economic costs associated with experimental testing [31].

QSAR models are a computational tool used to correlate the chemical structure of compounds with their biological activity. By analyzing the physicochemical properties of a large dataset of known anti-ulcer agents, QSAR models can identify structural features responsible for high bioactivity and predict the activity of novel compounds. This approach is particularly valuable for guiding the design of new anti-ulcer agents derived from natural sources, as it can optimize compounds for enhanced efficacy and minimal toxicity. Additionally, QSAR modeling can aid in the selection of solvent systems and reaction conditions that align with green chemistry principles, ensuring that the development process remains sustainable [32].

Docking studies, another key computational tool, simulate the interaction between natural compounds and their biological targets, such as enzymes or receptors involved in ulcer formation. By predicting the binding affinity and orientation of compounds within the active site of these targets, docking studies provide valuable insights into the mechanisms of action and help prioritize compounds with the most promising therapeutic profiles. In the context of anti-ulcer drug discovery, docking can identify natural compounds that effectively block the proton pump, inhibit *H. pylori* adhesion, or promote mucosal healing. Moreover, docking studies allow for the exploration of synergistic effects between compounds, enabling the design of combination therapies [33].

By integrating green chemistry principles into computational approaches, researchers can optimize the drug discovery process while minimizing the environmental impact. For instance, computational techniques can be used to predict the most efficient and eco-friendly synthetic routes for producing bioactive compounds. Additionally, the identification of non-toxic solvents and reagents for synthesis, based on computational predictions, further reduces the ecological footprint of drug development. Thus, computational tools not only streamline the discovery of effective anti-ulcer agents but also ensure that their development is aligned with sustainable and eco-friendly practices [34].

The limitations of current green chemistry approaches with respect to anti-ulcer drug discovery

While green chemistry approaches have significantly advanced the discovery and development of anti-ulcer compounds, several limitations still exist, particularly in their application to natural product-based drug discovery. One major challenge is the complexity and variability of natural sources. Plant-derived compounds often exhibit a high degree of structural diversity, making their extraction and synthesis difficult to standardize. This variability can lead to inconsistent yields, bioactivity, and purity, even when green extraction methods like supercritical fluid extraction (SFE) or microwave-assisted extraction (MAE) are used. Furthermore, natural sources may contain a mixture of compounds, making it challenging to isolate and identify the specific bioactive components responsible for anti-ulcer activity [36].

Another limitation is the scalability of green extraction techniques. While methods like SFE and MAE are highly efficient at the laboratory scale, they may not always be cost-effective or scalable for industrial production. For example, supercritical CO₂ extraction requires specialized equipment and operational costs that may not be feasible for large-scale applications. Similarly, while green solvents such as ethanol or water are used in some methods, their application on a commercial scale still faces challenges in terms of solvent recovery, solvent loss, and energy requirements [37].

Regulatory and safety concerns also present a challenge. While green chemistry promotes the use of non-toxic, eco-friendly solvents, many natural compounds derived from plants require extensive validation to meet regulatory standards. The process of ensuring that these compounds are safe and effective for clinical use can be time-consuming and costly, particularly when working with natural products whose pharmacokinetics and toxicity profiles are not fully understood [37].

Lastly, lack of standardization in analytical methods is another constraint in green chemistry applications. With numerous natural compounds to test, researchers often face difficulties in analyzing and quantifying active ingredients. Traditional analytical techniques like HPLC or GC-MS, although highly effective, are not always adapted for high-throughput screening in green chemistry, which could limit their applicability in large-scale discovery [38].

Future directions for green chemistry in natural compound development

Despite these limitations, the future of green chemistry in natural compound-based drug discovery, particularly for anti-ulcer agents, holds great promise. One key direction is the advancement of more efficient and scalable green extraction methods. Research is focused on improving existing techniques such as SFE and MAE to reduce energy consumption, lower operational costs, and increase the yield and purity of bioactive compounds. Additionally, the development of green solvents that are both effective in extraction and safe for human consumption could further expand the applicability of green chemistry principles in pharmaceutical manufacturing [39].

Another promising area is the integration of artificial intelligence (AI) and machine learning (ML) into the green chemistry process. These technologies can optimize extraction parameters, predict the bioactivity of natural compounds, and identify new lead compounds with anti-ulcer properties. AI/ML can analyze large datasets from high-throughput screening and computational studies to predict compound efficacy, toxicity, and other important pharmacological properties, helping to streamline the drug discovery process while reducing environmental and resource costs [40].

Incorporating multi-disciplinary approaches, including biotechnology, bioinformatics, and green chemistry, will also be critical in advancing natural product drug development. For instance, synthetic biology could be used to engineer microorganisms that produce plant-derived compounds more efficiently, reducing the need for large-scale cultivation and traditional extraction methods. Advances in metabolic engineering could enable the production of bioactive compounds in more sustainable systems, such as genetically modified microorganisms or algae, further reducing the environmental impact associated with plant-based extractions [41].

Another future direction is the standardization and optimization of analytical techniques for high-throughput green screening. The development of more sensitive, automated, and eco-friendly analytical tools could significantly enhance the ability to monitor the quality and purity of natural extracts, ensuring that green methods are viable for large-scale production. Moreover, the integration of *in silico* modeling in the early stages of drug development could reduce the reliance on traditional, resource-intensive experimental techniques by predicting the best extraction conditions and potential bioactive compounds [38].

Finally, collaboration across industries will be vital in overcoming the current limitations of green chemistry in natural product-based drug discovery. Collaborative efforts between academia, industry, and regulatory bodies could facilitate the development of more efficient, scalable, and sustainable methods for the extraction, synthesis, and testing of anti-ulcer agents from natural sources. As the field of green chemistry continues to evolve, it holds the potential to provide sustainable, eco-friendly, and highly effective solutions for the treatment of ulcers and other gastrointestinal diseases [42].

Significance of integrating green chemistry with natural product research

Integrating green chemistry with natural product research holds profound significance in the development of sustainable and effective therapeutic agents, especially in the context of anti-ulcer drug discovery. Green chemistry principles, with their focus on reducing environmental impact, enhancing resource efficiency, and improving safety, align perfectly with the growing need for eco-friendly, cost-effective, and health-conscious pharmaceutical solutions. Natural products, derived from plants, fungi, and microorganisms, have historically been a rich source of bioactive compounds with promising medicinal properties. However, traditional methods of isolation and synthesis often rely on hazardous chemicals, energy-intensive processes, and non-renewable resources, which are not sustainable in the long term [43].

By applying green chemistry principles, such as using renewable feedstocks, non-toxic solvents, and energy-efficient techniques, the extraction and synthesis of natural products can be made more environmentally friendly, thus addressing many of the ecological concerns associated with pharmaceutical production. Green extraction methods like supercritical fluid extraction (SFE) and microwave-assisted extraction (MAE) have already demonstrated their ability to enhance yields, preserve bioactivity, and reduce harmful byproducts. Moreover, the use of computational tools like QSAR modeling and docking studies helps in optimizing the biological activity of natural compounds while minimizing the reliance on experimental methods that require large amounts of resources [44].

The synergy between green chemistry and natural product research also promises to reduce the time and cost involved in drug discovery, which is crucial in meeting the ever-growing demand for safe and effective medicines. As we seek alternatives to synthetic drugs, particularly in areas such as anti-ulcer therapies, integrating green chemistry ensures that these solutions are both sustainable and scalable, making them suitable for global pharmaceutical markets [45].

Conclusion

The integration of green chemistry with natural product research is still in its early stages, and much remains to be explored to unlock the full potential of this interdisciplinary field. There is a need for continued innovation in green extraction techniques that can be applied not only to small-scale laboratory research but also to large-scale commercial production. The development of new eco-friendly solvents and the optimization of extraction conditions that preserve the bioactivity of natural compounds while minimizing waste should be prioritized in future research.

Additionally, advances in computational approaches offer significant opportunities to streamline drug discovery processes. Research should focus on refining QSAR models, molecular docking techniques, and other in silico tools to predict the efficacy and safety of natural compounds before they enter the costly and resource-intensive stages of experimental validation. This predictive modeling can accelerate the identification of lead compounds and enable a more sustainable approach to drug development.

Furthermore, collaborative research efforts between academic institutions, pharmaceutical industries, and environmental organizations are critical to overcoming the challenges that currently limit the scalability and effectiveness of green chemistry approaches. Interdisciplinary collaboration can lead to innovations in both the biological and chemical aspects of drug discovery, creating a holistic approach that balances ecological sustainability with therapeutic efficacy.

As the world continues to confront environmental challenges and rising healthcare needs, it is essential to foster a research environment that prioritizes sustainable pharmaceutical development. Green chemistry, when integrated with natural product research, provides a compelling solution to creating medicines that are not only effective and safe but also environmentally responsible. Further research in this field is imperative for the discovery of novel anti-ulcer agents and other therapeutic compounds that will benefit both human health and the planet. The time is now to invest in and prioritize this exciting interdisciplinary field, where sustainability and innovation converge for the greater good.

References

1. Serafim, C., et al., *A Review of the Role of Flavonoids in Peptic Ulcer (2010-2020)*. Molecules, 2020. **25**(22).
2. Salih, B.A., et al., *H pylori infection and other risk factors associated with peptic ulcers in Turkish patients: a retrospective study*. World J Gastroenterol, 2007. **13**(23): p. 3245-8.
3. Houglum, J.E., G.L. Harrelson, and T.M. Seefeldt, *Drugs for Treating Gastrointestinal Disorders, in Principles of Pharmacology for Athletic Trainers*. 2024, Routledge. p. 186-209.
4. Elnour, A.A.M. and N.H. Abdurahman, *Current and potential future biological uses of Saussurea costus (Falc.) Lipsch: A comprehensive review*. Heliyon, 2024. **10**(18): p. e37790.
5. Rahman, M.M., et al., *Natural therapeutics and nutraceuticals for lung diseases: Traditional significance, phytochemistry, and pharmacology*. Biomedicine & Pharmacotherapy, 2022. **150**: p. 113041.
6. Ramakrishna, V., B. Malleswari, and R. Ramagundam, *Green Chemistry Plays Key Role in Eco-Friendly, Sustainable Development*. 2020. **7**: p. 4024 to 4028.
7. Das, A.K., R. Chakraborty, and M. de la Guardia, *Teaching Green Analytical and Synthesis Chemistry: Performing Laboratory Experiments in a Greener Way*. Green Analytical Chemistry: Past, Present and Perspectives, 2019: p. 45-74.
8. Akram, M., et al., *Exploring the Frontiers of green nanotechnology: Advancing biomedicine, Herbonanoceuticals, environment, and sustainability*. Scicom Journal of Medical and Applied Medical Sciences, 2023. **2**(1): p. 18-30.
9. Warner, J.C., A.S. Cannon, and K.M. Dye, *Green chemistry*. Environmental Impact Assessment Review, 2004. **24**(7): p. 775-799.
10. Fuente-Ballesteros, A., et al., *Green sample preparation methods for the analysis of bioactive compounds in bee products: A review*. Advances in Sample Preparation, 2023. **6**: p. 100060.
11. Cheriyan, B.V., et al., *Eco-Friendly Extraction Technologies: A Comprehensive Review of Modern Green Analytical Methods*. Sustainable Chemistry for Climate Action, 2024: p. 100054.
12. Uwineza, P.A. and A. Waśkiewicz, *Recent Advances in Supercritical Fluid Extraction of Natural Bioactive Compounds from Natural Plant Materials*. Molecules, 2020. **25**(17).
13. Mungwari, C.P., et al., *Conventional and Modern Techniques for Bioactive Compounds Recovery from Plants: Review*. Scientific African, 2024: p. e02509.
14. Shinkar, A.S., *Phytochemical investigation and antiulcer activity of Aphanamixis polystachya (Wall.) Parker*. 2007, Rajiv Gandhi University of Health Sciences (India).
15. Vollmannová, A., et al., *Quercetin as one of the most abundant represented biological valuable plant components with remarkable chemoprotective effects - A review*. Heliyon, 2024. **10**(12): p. e33342.
16. Lu, J.J., et al., *Alkaloids isolated from natural herbs as the anticancer agents*. Evid Based Complement Alternat Med, 2012. **2012**: p. 485042.

17. Bojović, D., et al., *Summary of the phytochemical research performed to date on Sideritis species*. 2011.
18. Périco, L.L., et al., *Systematic Analysis of Monoterpenes: Advances and Challenges in the Treatment of Peptic Ulcer Diseases*. Biomolecules, 2020. **10**(2).
19. Ahmed, S.R., et al., *Therapeutic promises of medicinal plants in Bangladesh and their bioactive compounds against ulcers and inflammatory diseases*. Plants, 2021. **10**(7): p. 1348.
20. da Silva, R.F., et al., *Sustainable extraction bioactive compounds procedures in medicinal plants based on the principles of green analytical chemistry: A review*. Microchemical Journal, 2022. **175**: p. 107184.
21. Chemat, F., M.A. Vian, and G. Cravotto, *Green extraction of natural products: concept and principles*. Int J Mol Sci, 2012. **13**(7): p. 8615-8627.
22. Nayak, N., et al., *Advances in the novel and green-assisted techniques for extraction of bioactive compounds from millets: A comprehensive review*. Heliyon, 2024. **10**(10): p. e30921.
23. Bhadange, Y.A., J. Carpenter, and V.K. Saharan, *A Comprehensive Review on Advanced Extraction Techniques for Retrieving Bioactive Components from Natural Sources*. ACS omega, 2024. **9**(29): p. 31274-31297.
24. Tsim, K.W., *The functional diversity of flavonoids from Chinese medicines-Development of health food supplements for health promotion and disease prevention*.
25. Kim, H.J. and K.Y. Yoon, *Optimization of ultrasound-assisted deep eutectic solvent extraction of bioactive compounds from pomegranate peel using response surface methodology*. Food Sci Biotechnol, 2023. **32**(13): p. 1851-1860.
26. Carreira-Casais, A., et al., *Benefits and Drawbacks of Ultrasound-Assisted Extraction for the Recovery of Bioactive Compounds from Marine Algae*. Int J Environ Res Public Health, 2021. **18**(17).
27. Awad, A.M., et al., *Green Extraction of Bioactive Compounds from Plant Biomass and Their Application in Meat as Natural Antioxidant*. Antioxidants (Basel), 2021. **10**(9).
28. Ayon, N.J., *High-Throughput Screening of Natural Product and Synthetic Molecule Libraries for Antibacterial Drug Discovery*. Metabolites, 2023. **13**(5).
29. Di Gioia, S., M.N. Hossain, and M. Conese, *Biological properties and therapeutic effects of plant-derived nanovesicles*. Open Medicine, 2020. **15**(1): p. 1096-1122.
30. Begg, M., et al., *Comparing the Safety and Efficacy of Proton Pump Inhibitors and Histamine-2 Receptor Antagonists in the Management of Patients With Peptic Ulcer Disease: A Systematic Review*. Cureus, 2023. **15**(8): p. e44341.
31. Shah, M., et al., *Computational transformation in drug discovery: A comprehensive study on molecular docking and quantitative structure activity relationship (QSAR)*. Intelligent Pharmacy, 2024. **2**(5): p. 589-595.
32. Asirvatham, S., B.V. Dhokchawle, and S.J. Tauro, *Quantitative structure activity relationships studies of non-steroidal anti-inflammatory drugs: A review*. Arabian Journal of Chemistry, 2019. **12**(8): p. 3948-3962.
33. Asiamah, I., et al., *Applications of molecular docking in natural products-based drug discovery*. Scientific African, 2023. **20**: p. e01593.
34. Singh, B., et al., *Pharmaceutical advances: Integrating artificial intelligence in QSAR, combinatorial and green chemistry practices*. Intelligent Pharmacy, 2024. **2**(5): p. 598-608.
35. Jawarkar, R.D., et al., *Cheminformatics approaches to predict the bioactivity and to discover the pharmacophoric traits crucial to block NF- κ B*. Chemical Physics Impact, 2024. **9**: p. 100720.
36. Berida, T.I., et al., *Plant antibacterials: The challenges and opportunities*. Heliyon, 2024. **10**(10): p. e31145.
37. Cannavacciuolo, C., et al., *Critical analysis of green extraction techniques used for botanicals: Trends, priorities, and optimization strategies-A review*. TrAC Trends in Analytical Chemistry, 2024. **173**: p. 117627.
38. Bashir, N., et al., *Chapter Fifteen - Future of analytical chemistry in relation to the green nanoparticles*, in *Comprehensive Analytical Chemistry*, C. Mustansar Hussain, Editor. 2024, Elsevier. p. 419-460.
39. Huang, L., et al., *The development of nanocarriers for natural products*. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 2024. **16**(3): p. e1967.
40. Tripathi, P., et al., *Chapter Two - Implementation of artificial intelligence (AI) and machine learning (ML) in microbiology*, in *Methods in Microbiology*, A. Srivastava and V. Mishra, Editors. 2024, Academic Press. p. 29-41.
41. David, F., et al., *A Perspective on Synthetic Biology in Drug Discovery and Development—Current Impact and Future Opportunities*. SLAS Discovery, 2021. **26**(5): p. 581-603.
42. Iles, A. and M. Mulvihill, *Collaboration Across Disciplines for Sustainability: Green Chemistry as an Emerging Multistakeholder Community*. Environmental science & technology, 2012. **46**: p. 5643-9.

43. Zhu, Y., et al., *New opportunities and challenges of natural products research: When target identification meets single-cell multiomics*. Acta Pharmaceutica Sinica B, 2022. **12**(11): p. 4011-4039.
44. Ahmad, S., et al., *Recent advances in green chemistry approaches for pharmaceutical synthesis*. Sustainable Chemistry One World, 2024. **4**: p. 100029.
45. Atanasov, A.G., et al., *Discovery and resupply of pharmacologically active plant-derived natural products: A review*. Biotechnology Advances, 2015. **33**(8): p. 1582-1614.