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Natural Products and Phytochemicals in Modern Drug Discovery: Mechanistic Insights, Barriers, and Future Opportunities

Zahid Ali[1], Pallavi Chandel[1 *], Achla Sharma[1], Mohita Thakur[1], Firdosa Akhter[1].

[1]School of Pharmacy, Deshbhagat University, off to NH-44, Amloh Road, Mandi Gobindgarh District Fatehgarh Sahib, Punjab- 14, Mandi Gobindgarh, Punjab 147301, India.

ABSTRACT

Natural products have long been central to therapeutic development, offering structurally diverse compounds that continue to inspire modern drug discovery. Phytochemicals including polyphenols, flavonoids, terpenoids, and alkaloids exert multi-target actions that regulate oxidative stress, inflammation, apoptosis, and immune and metabolic pathways. These pleiotropic effects make them promising candidates for treating complex, multifactorial diseases such as cancer, cardiovascular disorders, diabetes, and neurodegenerative conditions. Despite their therapeutic potential, the clinical progression of natural products is restricted by poor solubility, low bioavailability, metabolic instability, and variability arising from environmental and seasonal factors. Limited standardization and insufficient large-scale clinical trials further impede regulatory approval.Recent technological advances are helping overcome these limitations. Modern extraction techniques, advanced chromatographic and spectroscopic profiling, structural modification strategies, nanocarrier-based delivery systems, and synthetic biology platforms have improved the stability, yield, and pharmacokinetic performance of natural compounds. Omics-driven analyses and computational modelling have enhanced understanding of molecular mechanisms and facilitated more efficient identification and optimization of bioactive leads.By integrating traditional pharmacognosy with emerging scientific innovations, natural products and phytochemicals remain vital contributors to future drug discovery, offering sustainable, mechanistically rich, and clinically relevant avenues for therapeutic development.

Keywords: ***Natural products, Phytochemicals, Drug discovery, Bioavailability, Nanotechnology, Synthetic biology.***

***Corresponding Author:**
Miss. Pallavi Chandel
School of Pharmacy, Desh Bhagat University, off to NH-44, Amloh Road, Mandi Gobindgarh District Fatehgarh Sahib, Punjab- 14, Mandi Gobindgarh, Punjab 147301, India
Email; pallavichandel1921@gmail.com
ORCID ID: 0009-0000-5819-6016

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1. Introduction

Medicinal and pharmacological science has been built upon natural products since time immemorial and has provided structurally diverse molecules which have dictated traditional and modern therapeutic paradigms [1]. Plant-based remedies were used widely in ancient societies around the world, such as the

Egyptians, the Chinese, the Indians, the Greeks, and the Indigenous groups, to cure a wide range of diseases, including infectious diseases and inflammatory diseases, as well as metabolic diseases, neurological diseases, and wounds [2]. The traditional medicine tradition like Ayurveda, Traditional Chinese Medicine (TCM), Unani, and the Indigenous medicine used complex herbal preparations which were mixtures of various botanical species to have synergistic therapeutic effects. The activity of these conventional remedies was frequently dependent on the complexity of interactions between bioactive constituents, many of which remain still significant in the modern drug discovery [3].

The contribution of natural products to modern medicine is demonstrated by some of the landmark drugs. Aspirin, a compound of Salix alba (willow bark), changed the approach to the treatment of pain and cardiovascular care because it has been shown to reduce inflammation and thrombosis by inhibiting the activity of cyclooxygenase (COX) enzymes [4]. Morphine, a compound of opium poppy (Papaver somniferum), became the standard of analgesia in severe pain, and artemisinin, which was a compound of artemisia annua, changed malaria treatment by offering very effective antimalarial therapy as well as minimizing resistance development [5]. Other striking ones are such as paclitaxel, a diterpenoid alkaloid of Taxus brevifolia, which is still the workhorse of cancer chemotherapy, and vincristine and vinblastine which are alkaloids of Catharanthus roseus [6], which inhibits tumour growth by targeting microtubule dynamics. These achievements demonstrate the timeless usefulness of natural products as structural useful, biologically active molecules that have remained useful as models of how to design synthetic analogues and combinatorial drug development [7].

The most promising natural products include phytochemicals, which are defined as secondary products produced by plants. The major types of phytochemicals are polyphenols, flavonoids, terpenoids, alkaloids, saponins and coumarins, with a wide range of chemical structures and wide range of biological functions [8]. Phytochemicals have multi-target, pleiotropic properties and can regulate oxidative stress, inflammatory signalling, apoptotic pathways, and immune responses at the same time unusual to conventional synthetic drugs, which generally act on only one molecular target [9]. The SIRT1 and AMP-activated protein kinase (AMPK) are activated by resveratrol, which is a grape stilbene polyphenol, and improves mitochondrial activity, antioxidant defences, and metabolic control [10]. Quercetin Applications Quercetin is a flavonoid that stays oncogenic and inhibits the synthesis of inflammatory cytokines, alters PI3K/Akt signal, and causes apoptosis in cancer cells. Terpenoids such as Boselli acids and ginsenosides exhibit anti-inflammatory, neuro-protective and anticancer effects whereas alkaloids such as calprotectin and vincristine interact with topoisomerases and microtubules to exert a cytotoxic effect in tumours [11]. This multi-target profile makes Phyto-chemicals especially useful in the treatment of more complex, multifactorial diseases like cancer, diabetes, cardiovascular diseases, neuro-degeneration, and autoimmune diseases where dysregulation of a number of signalling pathways may be involved [12].

Although Phyto translations have the potential to offer a promising therapeutic option, there are significant challenges encountered in translating phytochemicals into clinically viable drugs. In-vivo efficacy is significantly compromised by pharmacokinetic limitations, which are low solubility, poor bioavailability, rapid metabolism, and chemical in-stability [13]. In addition, geographic and seasonal changes in the flora make standardization and reproducibility of extracts more challenging, which are essential points of approval by the regulatory. Mechanism of action of multi-component extracts is a concept in itself that is complex to explain, and the absence of effective intellectual property protection often discourages pharmaceutical business [14]. Lastly, there are limited clinical trials that rigorous clinical trials would have validated evidence-based efficacy and safety and further increased the gap between preclinical research and clinical practice [15].

liposomes, polymeric nanoparticles, dendrimers, and solid lipid nanoparticles improve bioavailability and solubility as well as targeting phytochemicals and reducing overall toxicity in the body [16]. Computational drug design, molecular docking, quantitative structureactivity relationship (QSAR) modelling and artificial intelligence are useful in high-throughput screening, target prediction, and rational optimisation of bioactive molecules [17]. The insights into polypharmacological mechanisms, network pharmacological interactions, and identification of biomarkers are produced by omics-based studies, which encompass genomics, transcriptomics, proteomics, and metabolomics [18]. Synthetic biology lets provide scalable, sustainable microbial bio-synthesis of phytochemicals, and thus bypass environmental and seasonal constraints and allow structural engineering to increase pharmacokinetic properties and therapeutic activity [19] The aim of the review is to provide the evaluation of natural products and phytochemicals in the framework of modern drug discovery. It attempts to question mechanistic understanding, to document progress in separation and structural streamlining, to define barriers to clinical transfer, to evaluate developing approaches that get

over these difficulties, and to define future opportunities of sustainable, effective, and precision therapeutics [20]. Through the combination of past pharmacognosy with the new scientific innovation, phytochemicals will continue to serve as a part of the next generation drug discoveries and global medicine and, in doing so, will reconcile millennia of botanical knowledge with the technological revolution [21].

2. Mechanistic Insights of Natural Products and Phytochemicals

The mechanism of therapeutic efficacy of natural products and their constituent phytochemicals results from complex, multi-target mechanisms that are orchestrated in a wide variety of cellular processes implicated in disease pathogenesis [22]. Phytochemicals cause pleiotropic effects, involving the modulation of oxidative stress, inflammation, apoptosis, autophagy, mitochondrial dynamics, immune responses and signalling cascades, whereas conventional synthetic agents usually interact with one particular receptor and/or enzyme. Consequently, this multi-target profile provides tremendous therapeutic benefit in chronic, multi-factorial diseases such as oncologic, cardiovascular, metabolic, neurodegenerative and autoimmune diseases [23].

Oxidative stress, which is characterized by superabundant production of reactive oxygen species (ROS), is a basis of cellular damage, chronic inflammation, senescence, and disease progression. Events of oxidative stress are mitigated by phytochemicals due to direct antioxidant action as well as endogenous stimulation through phytochemicals. Polyphenols, flavonoids, terpenoids directly neutralise free radicals and so prevent lipid peroxidation, protein oxidation and damage to DNA [24]. Resveratrol and curcumin increase the transcription factor nuclear factor erythroid 2- related factor (Nf2) which in turn increases the expression of antioxidant enzymes including superoxide dismutase (SOD), catalase and glutathione peroxidase. Epigallocatechin-3-gallate Epigallocatechin 3 gallate (EGCG) is a catechin derivative from green tea that enhances mitochondrial biogenesis and protects against oxidative injury in cardiomyocytes and neurons. These antioxidant mechanisms constitute neuro- and cardioprotection and chemoprevention strategies [25].

Sero-inflammasomes form an underlying pathologic process in a range of diseases such as cancer, type II + diabetes, neurodegenerative diseases, and atherosclerosis. Phytochemicals blunt inflammatory response by regulating transcription factors, cytokine patterns as well as enzymatic mediators [26]. For example, curcumin blocks the nuclear factor-kappa B (NF-kappa B) signalling pathway so prevents the production of pro-inflammatory cytokines, such as tumour necrosis factor alpha (TNF-alpha), interleukin (IL)-6 and IL -1-beta (IL-1-beta) [5]. Endothelial inflammation is relieved by quercetin by inhibiting adhesion molecules and chemokine expression. Terpenoid Compounds, exemplified by Boswellia acids suppress leukotrienes production through down-regulation of 5-lipoxygenase and phospholipase A2. These anti-lowering capacity actions not only prevent chronic tissue damage but also lead to inflammation resolution, making phytochemicals viable adjuvants or even alternatives to the conventional anti-lowering therapeutics [27].

Phytochemicals are often active on apoptotic pathways and cell-cycle checkpoints and therefore interfere with anticancer activity. Flavonoids such as quercetin and genistein induce caspase dependent apoptosis, increase expression of pro-apoptotic proteins (e.g. Bax) and decrease expression of anti-apoptotic proteins (e.g. Bcl-2), thereby inducing programmed cell death in malignant cells [28]. Curcumin induces cell cycle arrest at G1/S and G2/M checkpoint by modulating cyclins and cyclin dependent kinases thus preventing abnormal proliferation of cells. Alkaloid constituents such as apothecia block topoisomerase I and cause DNA-strand breaks and apoptosis. These mechanistic actions harbour the potential to increase the efficacy of standard chemotherapeutic regimens when used in combination, whilst concurrently reducing the systemic toxicity [29].

Figure 1 depicts the mechanistic pathways of major phytochemicals: curcumin, resveratrol, and quercetin, highlighting their antioxidant activation through the Nrf2-ARE pathway, suppression of inflammatory mediators via NF-κB and MAPK inhibition, and induction of apoptosis through modulation of caspases and mitochondrial pathways. The diagram visually integrates these multi-target actions to demonstrate how phytochemicals collectively reduce oxidative stress, control inflammation, and promote programmed cell death [30].

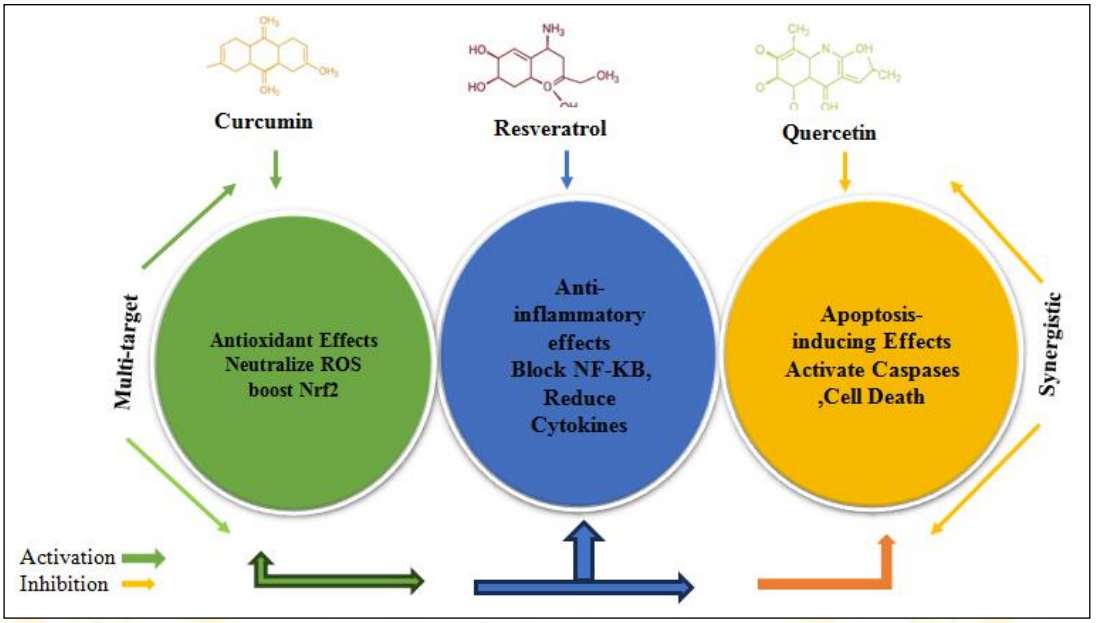

Figure 1: Mechanistic pathways of key phytochemicals (e.g., curcumin, resveratrol, quercetin) showing antioxidant, anti-inflammatory, and apoptosis-inducing effects.

3. Advances in Isolation, Characterization, and Structural Modification

Significant advances have been made in the isolation, characterization, and structural modification of natural products and phytochemicals. Modern extraction techniques, sophisticated analytical methods, structure-optimization strategies, and state-of-the-art computational tools now work in concert to accelerate the discovery pipeline [31]. These innovations enable the identification of bioactive compounds with improved therapeutic profiles and enhanced clinical potential. Traditionally bioactive compounds were extracted by using conventional methods such as maceration, Soxhlet extraction, percolation and decoction [32]. Although these methods have been useful, they were limited by lower yields, possible thermolabile constituent degradation, prolonged extraction times, high solvent use and lack of reproducibility. As the precision and scalability required in drug discovery has increased, new extraction and characterisation protocols have been designed to overcome these issues [33].

The new generation of extraction techniques complement yield, selectivity, and structural integrity of the phytochemical. Key approaches include Ultrasound-Assisted Extraction (UAE) which enables disruption of cell walls in plants with high frequency ultrasound waves leading to an increased penetration of solvent for extraction and improved extraction efficiency while minimising both extraction time, solvent consumption and thermal loss of sensitive compounds [34]. Microwave-Assisted Extraction (MAE) employs microwave energy to rapidly heat the solvents and plant matrices to enhance diffusion of the target molecules with minimum degradation and reduced energy consumption [35]. Supercritical Fluid Extraction (SFE) involves supercritical CO2 as a green and non-toxic solvent, allowing adjustable parameters of temperature and pressure that allow for high selectivity and follow the green chemistry principles [36]. Pressurised Liquid Extraction (PLE) uses an accelerated extraction under high pressure and temperature and provides faster, more reproducible, and efficient extractions especially for thermally stable compounds and high throughput applications. These advanced methodologies not only enhance overall yield, but also maintain the integrity of the bioactive compounds, making them suitable for further pharmacological and clinical studies [35].

The analytical characterisation section outlines the procedures used by researchers to analyse data and the techniques employed. Comprehensive phytochemical profiling requires careful quality evaluation to support drug discovery and approval. Modern analytical platforms offer the ability to profile complex plant extracts in detail and combine chromatography, mass spectrometry, nuclear magnetic resonance and metabolomics [37]. Chromatographic separation and quantification of phytochemicals from complex matrices are achieved regularly by high-performing liquid chromatography (HPLC), ultra-performing liquid chromatography (UPLC), gas chromatography (GC), and high performing thin layer chromatography (HPTLC) [38]. Mass Spectroscopy (MS) coupled with chromatography systems (LC - MS/MS, GC - MS) offers a precise molecular mass determination, structure determination and a thorough metabolite identification. Nuclear

Magnetic Resonance (NMR) Spectroscopy provides detailed structural information, such as stereochemistry and assignment of the functional groups, which are crucial for understanding biological interactions [39].

Metabolomics as an integrative analysis of secondary metabolites using a combination of chromatography, MS, NMR, and bioinformatic analyses provides the opportunity to perform a holistic profiling of secondary metabolites. This is enabling the identification of new compounds, mechanistic understanding of particular biological processes, and biomolecular activity and pharmacological result correlations [40]. Analytical characterisation can guarantee reproducibility, facilitate standardisation and allow correlation of chemical composition and therapeutic efficacy [41]. Phytochemicals have substantial bioactivity; but their pharmacokinetic profiles are often not optimal, which are marked by a low bioavailability, instability and solubility. Drug-like properties and therapeutic efficacy can be enhanced by structural modification such as semi-synthetic derivatization where functional groups can be optimized for better solubility, stability, and potency [42]. For example, the replacement of hydroxyl and methoxy functionalities in the analogues of curcumin has been reported to enhance both anticancer activity and pharmacokinetic performance. Synthetic derivatives of resveratrol with altered hydroxylation patterns exhibit improved bioavailability as well as greater cardiovascular and neuroprotective effects. Similarly, modification of alkaloids (e.g., vinblastine derivatives) can lead to enhancement of cytotoxicity and the simultaneous reduction of adverse side effects [43].

Prodrug strategies - conjugate of phytochemicals with hydrophilic carriers/polymers for improved solubility, absorption, and protection of biologic activity. Computational methods are being used for the faster discovery, optimization and elucidating the mechanism of phytochemicals [44]. Molecular docking is used to predict the binding affinity and to identify the interaction site of phytochemicals with their biological targets. Quantitative Structure-Activity Relationship (QSAR) modelling is a framework for rational chemical modification that can be used to achieve the desired goal of improving pharmacological activity whilst minimising toxicity [45]. Molecular dynamics simulation is used to assess the stability and conformational dynamics of phytochemicals in their targets. Artificial-intelligence based predictive modelling enables high throughput virtual screening and multiple target prediction, as well as lead optimization, reducing the experimental workload and cost [46].

The third phase is the importation of synthetic biology. This discipline provides the possibility to produce natural products on a large scale and in a sustainable way, by heterologous expression in engineered microorganisms such as Escherichia coli, Saccharomyces cerevisiae and Streptomyces spp. of pathways known from plant biosynthesis [47]. The benefits include high-yield, independent production throughout the year, the creation of novel analogues with better pharmacokinetic properties and improved environmental sustainability and cost-effectiveness [48].

Table 1 summarizes the key phytochemicals with well-established pharmacological relevance, highlighting their natural sources and validated molecular targets. Organizing these compounds in a comparative framework helps illustrate their multi-target mechanisms, enabling a clearer understanding of how natural products contribute to antioxidant, anti-inflammatory, neuroprotective, and chemopreventive pathways. Such a synthesis strengthens the rationale for utilizing phytochemicals as promising leads in modern drug discovery [49].

Table 1: Examples of Major Phytochemicals, Their Natural Sources, and Therapeutic Targets.

S. No	Phytochemical	Natural Source(s)	Chemical Class	Key Therapeutic Targets / Mechanisms	Major Biological Activities	References
1.	Curcumin	Curcuma longa (Turmeric)	Polyphenolic diketone	NF-κB, Nrf2/ARE pathway, COX-2, LOX, STAT3, TNF-α	Anti-inflammatory, antioxidant, anti-cancer, neuroprotective	[50]
2.	Resveratrol	Grapes, red wine, berries, peanuts	Stilbene polyphenol	SIRT1, AMPK, NF-κB, COX, ROS scavenging proteins	Anti-aging, cardio-protective, anti-inflammatory, anti-diabetic	[51]
3.	Quercetin	Onions, apples, citrus fruits, berries	Flavonol	MAPKs, PI3K/Akt, NF-κB, iNOS, IL-6 inhibition	Antioxidant, anti-inflammatory, antiviral, anti-allergic	[52]
3	Epigallocatechin-3-gallate (EGCG)	Green tea (Camellia sinensis)	Catechin	EGFR, VEGF, NF-κB, JAK/STAT, Bcl-2 family	Anti-cancer, antioxidant, metabolic regulation	[53]
4	Berberine	Berberis species,	Isoquinoline alkaloid	AMPK activation, NF-κB	Anti-microbial, anti-diabetic, anti-	[54]

		Goldenseal		suppression, NLRP3 inflammasome	inflammatory	
5	Ginsenosides (e.g., Rb1, Rg3)	Panax ginseng	Triterpenoid saponins	PI3K/Akt, Nrf2, NO synthase modulation	Neuroprotective, adaptogenic, immunomodulatory	[55]
6	Withanolides (e.g., Withaferin A)	Withaniasomnifera (Ashwagandha)	Steroidal lactones	NF-κB, Hsp90, Akt, vimentin	Anti-stress, anti-tumor, anti-inflammatory	[56]
7	Lycopene	Tomatoes, watermelon, red fruits	Carotenoid	Antioxidant ROS scavenging, IGF-1 inhibition	Anti-cancer (prostate), cardioprotective	[57]
8	Allicin	Garlic (Allium sativum)	Organosulfur compound	NF-κB, Nrf2, thiol-dependent enzymes	Anti-microbial, cardioprotective, antioxidant	[58]
9	Gingerol (6-Gingerol)	Zingiber officinale (Ginger)	Phenolic ketone	NF-κB, COX-2, TRPV1	Anti-inflammatory, analgesic, antioxidant	[59]
10	Apigenin	Parsley, chamomile, celery	Flavone	PI3K/Akt, NF-κB, Bcl-2 family, MAPKs	Anti-cancer, anxiolytic, anti-inflammatory	[60]
11	Boswellic acids	Boswellia serrata (Frankincense)	Triterpenoids	5-LOX inhibition, NF-κB suppression	Anti-arthritic, anti-inflammatory	[61]
12	Anthocyanins	Blueberries, blackberries, cherries	Flavonoid pigments	Nrf2 activation, inhibition of oxidative enzymes	Antioxidant, anti-aging, neuroprotective	[62]
13	Capsaicin	Chili peppers (Capsicum spp.)	Vanilloid alkaloid	TRPV1, Substance-P depletion	Analgesic, thermogenic	[63]
14	Silymarin (Silibinin)	Milk thistle (Silybum marianum)	Flavonolignan	Nrf2/Keap1, TGF-β, ROS-scavenging	Hepatoprotective, antioxidant	[64]

4. Barriers and Challenges in Natural Product Based Drug Discovery

Natural products have great potential as therapeutics; however, many barriers exist to the smooth flow of natural products into clinically viable therapeutics. Primarily their suboptimal solubility, insufficient bioavailability, and limited physicochemical stability often preclude adequate absorption, rapid dissemination throughout the body or sustained activities in biological surroundings [65]. As a result, many promising compounds break down too early or fail to reach a therapeutically relevant concentration at their target sites of action, reducing efficacy overall. An additional major hindrance lies in the complex processes involved with extraction, isolation and purification. Plant and microbial matrices typically have hundreds of structurally similar constituents making reproducible isolation of pure bioactive molecules difficult [66]. Geographical provenance, environmental variables and harvesting methodologies add to the mix, thus affecting the chemical composition and thus diminish the reproducibility. Regulatory and standardization issues are also playing a big role as barriers. Natural extracts are variable, developing quality, safety, and potency is difficult [67]

These complexities make regulatory approval more stringent than those for synthetic pharmaceuticals which have predictable chemical uniformity and therefore, are more easily assessed. Despite strong laboratory and preclinical data, natural compounds are often faced with sparse clinical translation [68]. Constraints including the lack of availability of adequate large scale trials, the challenges in funding, intellectual property aspects and composition variability of extracts hamper the progress from bench to bedside. Collectively, these challenges highlight the need for sophisticated analytical approaches, and improved delivery systems and conveyance of natural products for optimal conveyance of therapeutic value of derived natural products [69].

Figure 2 provides a schematic overview of the major barriers encountered throughout the natural product drug development pipeline from initial compound discovery and extraction challenges to issues of bioavailability, standardization, regulatory hurdles, and limited clinical translation. The diagram highlights

how each stage presents unique scientific, technical, and logistical obstacles that collectively slow the progression of natural products from laboratory research to approved therapeutics [70].

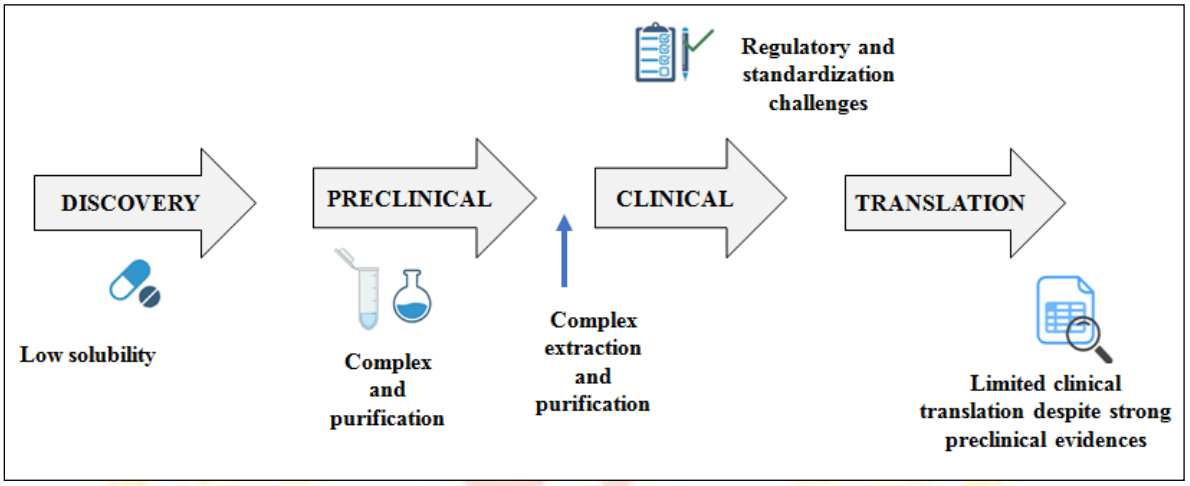

Figure 2: Schematic representation of barriers in natural product drug development pipeline (from discovery to clinical translation).

5. Overcoming Barriers: New Strategies

Although natural products provide a rich source of molecules for therapeutic intervention, desired drug molecules are generated through several challenges that have faced the field over the years [71]. Recent scientific and technological advances now provide innovative solutions to significantly increase the potential of natural products ansatz for drug discovery. One of the most efficacious strategies involves the development of nano formulations as well as sophisticated drug delivery systems [72]. Nanocarriers, such as liposomes, polymeric nanoparticles, nano emulsions, dendrimers, and solid lipid nanoparticles, significantly enhance phytochemical solubility, stability, and bioavailability as they are currently characterized by poor pharmacokinetic features. These delivery systems protect bioactive compounds against premature degradation, deliver a sustained release and allow for targeting to a specific tissue [73]. Such approaches not only enhance the efficacy of the therapy, they can also reduce the systemic toxicity, and in several cases have revived compounds that had been considered unsuitable for administration as part of the treatment due to unfavourable physicochemical characteristics [74].

A second promising avenue is with application of synthetic biology in sustainable, scalable production. Engineering microorganisms such as Escherichia coli, Saccharomyces cerevisiae, and Streptomyces helps in the biology of complex molecules found in nature without the need to depend on seasonal harvest of plants and endangered species [75]. Metabolic engineering and pathway reconstruction allows for higher yield, improved purity and even the production of structural analogues which display superior pharmacological properties. This strategy provides environmentally benign and economical alternative to the conventional forms of extraction [76]. To better understand the mode of action of natural compounds, an increasing number of researchers use the omics-driven approaches. Genomics, transcriptomics, proteomics and metabolomics together can contribute to the goal of the complete mapping of molecular targets, signalling cascades and biological networks modulated by phytochemicals [77]. These technologies reveal yet to be known mechanisms, markers of responses and optimize therapeutic applications. Integration of omics data with computational modelling also typically helps to speed up the elucidation of mechanisms and rational drug design [78].

Finally, synergistic formulations that combine natural products with synthetic agents have seen a growing interest. Such combinations can increase the therapeutic potency, overcome drug resistance and reduce adverse effects [79]. Natural compounds often affect the same cellular mechanisms as conventional agents, which makes it possible to use lower doses of synthetic drugs with the same or better efficacy [76].

6. Future Opportunities

Looking ahead, natural products and phytochemicals have a tremendous amount of promise for determining the next generation of therapeutic innovations. One of the most striking opportunities is in the role of these in the field(s) of precision medicine and personalised therapy [80]. As molecular profiling becomes even more accessible, it is now possible to correlate specific phytochemicals, or natural-product-derived compounds, with individual genetic, metabolic and epigenetic signatures. This customized approach can

provide amplified therapeutic responses and minimizing side effects and identify patient subsets most likely to respond to natural product-related therapeutic strategies [81]. Natural products are also being given a new spotlight due to their potential in immunotherapy and central nervous system (CNS) disorders. Many molecules from plant origin contain immunomodulatory actions that can complement the existing immunotherapies to enhance antitumor immunity or to suppress autoimmune responses [82]. Additionally, compounds with neuroprotective, anti-inflammatory and antioxidant properties may meet the multi-factorial pathogenesis of CNS diseases, against which single target synthetic drugs often fail. Consequently, natural molecules are promising candidates for e.g. Alzheimer's disease, Parkinson's disease, multiple sclerosis and several neuropsychiatric diseases [83]. The integration of AI and machine learning into natural product research - Another transformative prospect. AI-driven modelling for the expedited virtual screening, prediction of multi-target interactions, structural analogue identification for improved properties and rational optimisation Machine learning algorithms can also be used to analyse large datasets on omics data, which allows for more precise mechanism mapping and biomarker identification [84]. This paradigm of data-driven research significantly reduces timelines of discovery and improves the chances of making clinically relevant discovery leads. Finally, sustainable sourcing and green chemistry are proving to be an irreplaceable part of modern-day drug-sourcing [85]. Environmentally conscious methodologies of extraction, biocatalysis and renewable biosynthesis platforms to avoid ecological impact while ensuring the supply of bioactive compounds. These approaches strengthen the principles of ethical and sustainable development of drugs, especially of rare or slow growing medicinal plants [86].

Conclusion

Natural products and their phytochemical constituents continue to play a vital role in drug discovery, providing structurally diverse and biologically active compounds capable of influencing multiple disease-related pathways. Their antioxidant, anti-inflammatory, cytoprotective, and immunomodulatory effects offer therapeutic advantages that many single-target synthetic drugs cannot match. Yet, issues such as low bioavailability, chemical instability, variability in composition, and limited clinical evidence still hinder their progression into approved therapies.Recent developments—ranging from advanced extraction methods and improved analytical profiling to structural modification, nanotechnology-enhanced delivery systems, omics-based mechanistic studies, and sustainable biosynthetic production—are transforming the field. These innovations strengthen the pharmacological performance of phytochemicals and enable more reliable, scalable, and environmentally responsible development.The integration of natural products with precision medicine, synergistic formulations, and emerging biotechnologies presents a promising path for next-generation therapeutics. Progress will depend on continued interdisciplinary research, robust clinical validation, and sustainable sourcing practices. By uniting traditional pharmacognosy with modern scientific advances, natural products are positioned to remain a key driver of therapeutic innovation and global health improvement.

In summary, natural products and phytochemicals offer structurally diverse, multitarget compounds with significant therapeutic potential for complex diseases. Although challenges such as poor bioavailability, chemical instability, and limited standardization hinder their clinical translation, recent advances in extraction, analytical profiling, nanotechnology, and synthetic biology are helping overcome these barriers. These innovations improve pharmacokinetic performance, enhance mechanistic understanding, and support sustainable production. As scientific technologies evolve, natural products remain strong candidates for future drug development and precision therapeutics.

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