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HARNESSING PLANT BIOTECHNOLOGY FOR GENETIC RESILIENCE AND PHYTOCHEMICAL STABILITY IN HIGH-VALUE MEDICINAL CROPS: A REVIEW

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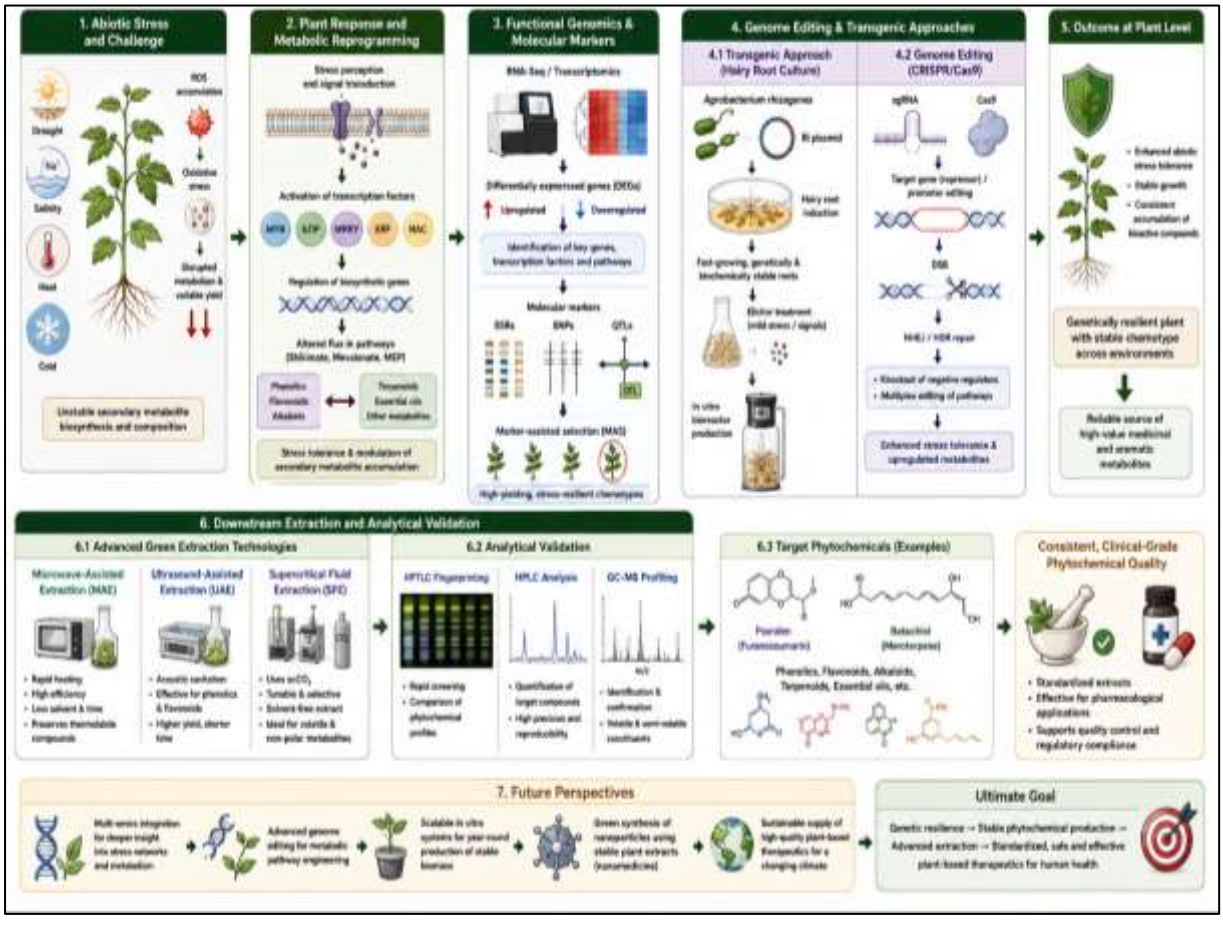
ABSTRACT

Global climate change severely threatens the phytochemical stability of medicinal and aromatic plants (MAPs) by disrupting secondary metabolite biosynthesis, compromising strict clinical standardization. This review examines the integration of functional genomics, marker-assisted selection (MAS), and CRISPR/Cas9 genome editing to engineer abiotic stress resilience in these critical crops. To ensure field-engineered resilience successfully translates to the laboratory, we evaluate advanced green extraction technologies, highlighting Microwave-Assisted Extraction (MAE) alongside analytical validation via HPLC and GC-MS. Using Psoralea corylifolia L. as a model, we demonstrate how precise extraction prevents the structural degradation of thermolabile bioactives like psoralen and bakuchiol. Finally, we explore the future of these stabilized extracts in nanobiotechnology, specifically their application in the green synthesis of silver nanoparticles for targeted anti-cancer therapeutics. Bridging precision molecular breeding with strictly calibrated downstream phytochemistry is essential for the sustainable, standardized production of plant-derived medicines.

KEYWORDS: Medicinal Crops; Abiotic Stress Tolerance; CRISPR/Cas9; Secondary Metabolites; Microwave-Assisted Extraction (MAE); Nanobiotechnology.

GRAPHICAL ABSTRACT



1. INTRODUCTION

Medicinal and aromatic plants (MAPs) are the foundational pillars of the global pharmaceutical, nutraceutical, and cosmetic industries, primarily cultivated for their secondary metabolites complex bioactive compounds such as alkaloids, terpenoids, and phenolics (Borah et al., 2024; Rout et al., 2000). These phytochemicals possess significant therapeutic properties, but their global supply chain is increasingly threatened by rapid climate change and extreme environmental fluctuations (Applequist et al., 2020; Mansinhos et al., 2024). Unlike primary metabolites that are essential for basic plant survival, the biosynthesis of secondary metabolites is highly responsive to environmental cues, acting as an ecological defense mechanism (Yang et al., 2018). While mild stress can sometimes act as an elicitor to upregulate certain beneficial compounds (Gorelick & Bernstein, 2014), severe or prolonged abiotic stresses such as drought, soil salinity, and extreme temperatures often disrupt metabolic pathways, leading to compromised plant biomass and highly erratic phytochemical yields (Isah, 2019; Yeshi et al., 2022).

Historically, agronomic advancements in MAPs have relied heavily on conventional breeding and standard cultivation practices. While these methods have successfully domesticated numerous species, they are inherently limited by narrow genetic bottlenecks and the protracted timeframes required to develop stable, stress-resistant cultivars (Kole et al., 2015). For specific high-value crops, such as Psoralea corylifolia, the consistency of key therapeutic compounds like psoralen and bakuchiol is heavily dependent on optimal environmental conditions (Alam et al., 2018). When conventional agronomy falls short in protecting these fragile biosynthetic pathways from climate volatility, securing crop viability requires intervening directly at the molecular level.

To bridge this gap, modern plant biotechnology offers unprecedented tools for establishing genetic resilience in aromatic and medicinal crops. Advances in functional genomics, transcriptomics, and multi-omics technologies now allow researchers to map the specific gene networks responsible for secondary metabolite production under stress conditions (Rai et al., 2017). Furthermore, genome-editing technologies, notably CRISPR/Cas9, alongside advanced in vitro transgenic approaches, present highly targeted strategies to precisely regulate the expression of key enzymes and transcription factors without altering the fundamental pharmacological profile of the crop (Espinosa-Leal et al., 2018; Zhu et al., 2020).

Therefore, this review aims to synthesize recent advancements in plant biotechnology dedicated to enhancing abiotic stress tolerance in MAPs. By evaluating molecular breeding strategies, genome-editing applications, and the subsequent stabilization of phytochemical profiles, this article highlights how genetic resilience at the nursery and field levels directly correlates with the standardized, high-quality yields required for advanced downstream pharmacological applications.

2. Impact of Abiotic Stress on Secondary Metabolite Biosynthesis

The biosynthesis of secondary metabolites in medicinal and aromatic plants (MAPs) is not a static process; rather, it is a highly dynamic ecological defense mechanism driven by continuous environmental interactions (Akula & Ravishankar, 2011; Hussein & El-Anssary, 2019). When subjected to abiotic stresses such as drought, extreme temperatures, and high soil salinity, plants typically undergo a fundamental physiological and metabolic shift (Krasensky & Jonak, 2012). According to the foundational Carbon-Nutrient Balance (CNB) hypothesis, when environmental constraints limit primary growth more heavily than photosynthesis, plants purposefully divert their accumulated carbon away from primary biomass production and channel it directly into secondary metabolic pathways (Peñuelas & Estiarte, 1998; Neilson et al., 2013). Consequently, environmental stressors directly dictate both the quantitative yield and the qualitative structural profile of therapeutic phytochemicals across varying growing seasons (Bourgaud et al., 2001).

At the cellular level, abiotic stress triggers the rapid overproduction of Reactive Oxygen Species (ROS), leading to severe oxidative stress, lipid peroxidation, and cellular degradation (Sharma et al., 2012; Hasanuzzaman et al., 2020). To mitigate this cellular damage, MAPs aggressively upregulate the synthesis of potent antioxidant compounds, primarily phenolics, flavonoids, and specific alkaloids, which serve as highly effective ROS scavengers (Kasote et al., 2015). Under controlled, mild stress conditions (e.g., regulated drought or moderate salinity), this precise physiological response can be harnessed as a deliberate agronomic strategy known as elicitation to artificially boost the concentration of target bioactive compounds prior to harvest (Valifard et al., 2014; Baenas et al., 2014). The metabolic pathways responsible for these compounds, such as the Shikimate pathway for aromatic amino acids and the Mevalonate pathway for isoprenoids, are frequently upregulated under stress, sharply increasing the accumulation of essential oils and specialized metabolites (Vranová et al., 2013; Punetha et al., 2022).

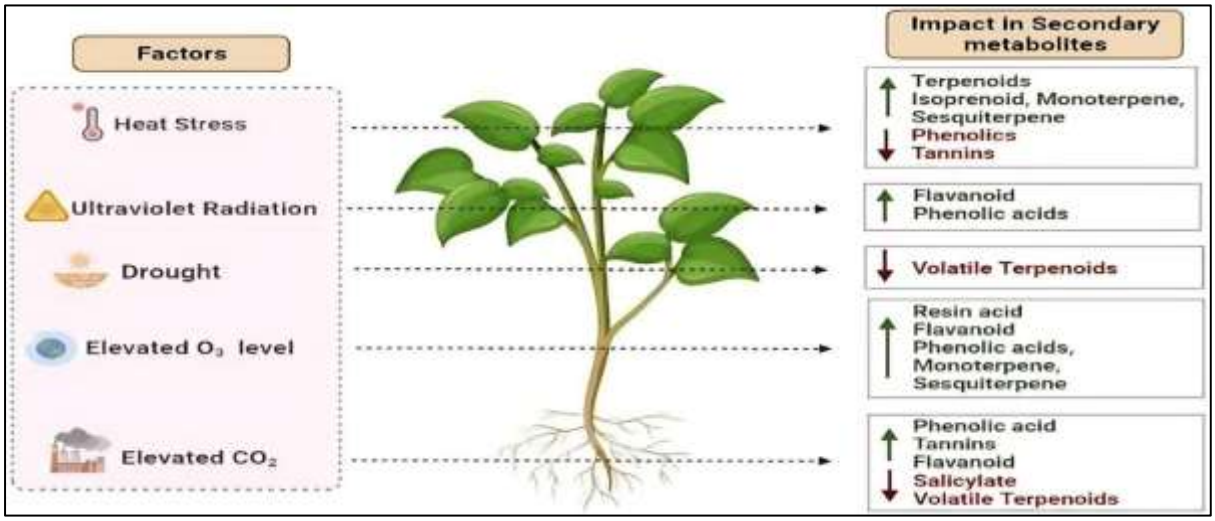


Figure 1. Modulation of secondary metabolite profiles in plants in response to diverse abiotic environmental stresses.

However, the threshold between stress-induced elicitation and metabolic collapse is remarkably narrow (Gorelick & Bernstein, 2014). Severe or prolonged abiotic stress forces MAPs into a critical survival mode where the intense metabolic cost of sustaining high levels of secondary metabolites becomes unsustainable for the plant's overall viability (Niinemets, 2016). Under extreme climatic volatility, the enzymatic activities within these biosynthetic pathways are heavily disrupted, leading to the rapid degradation of complex phytochemicals or the accumulation of unwanted, potentially toxic intermediates (Taiz et al., 2015).

This biochemical unpredictability poses a severe challenge for the commercial cultivation of high-value pharmacological crops like Psoralea corylifolia L. (Babchi) (Khushboo et al., 2010; Shaik et al., 2020). The therapeutic efficacy of P. corylifolia relies heavily on the precise ratios of its furanocoumarins, notably psoralen, and its meroterpenes, such as bakuchiol (Chaudhuri & Bojanowski, 2014; Alam et al., 2018). Because the transcription factors and enzymatic pathways governing the synthesis of these specific compounds are highly sensitive to fluctuating soil moisture and thermal stress, plants cultivated under erratic environmental conditions often yield highly inconsistent phytochemical profiles (Bhatia et al., 2013). Such biochemical instability directly compromises the strict pharmacological standardization required for modern clinical applications (Heinrich et al., 2020). This ultimately underscores the urgent need to embed genetic resilience directly into the plant's genome rather than relying solely on external, unpredictable agronomic management (Kole et al., 2015).

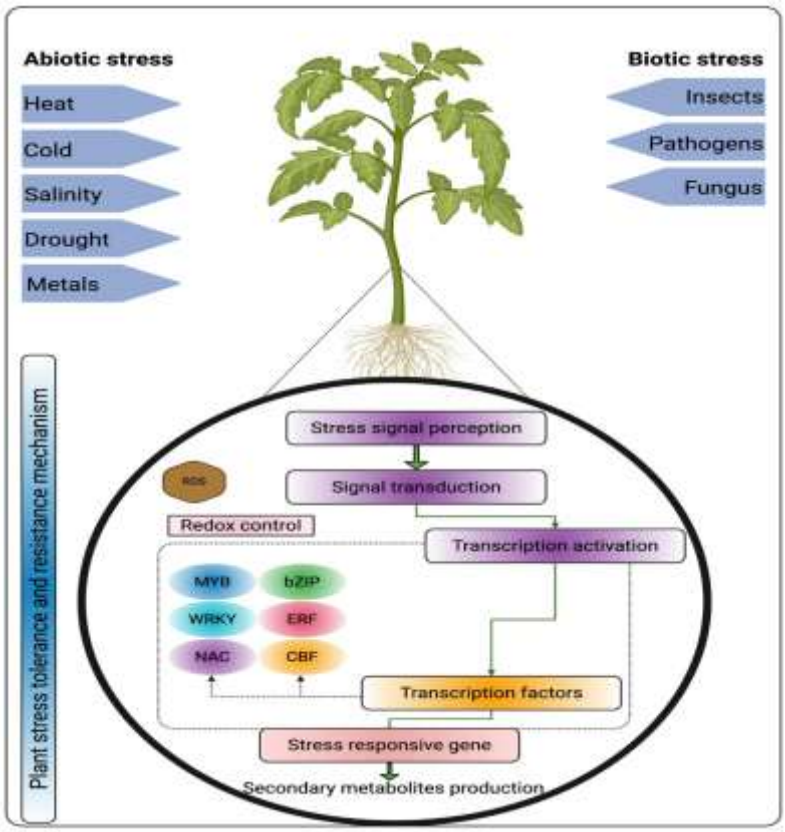


Figure 2. Molecular mechanisms underlying plant responses to biotic and abiotic stresses.

3. Functional Genomics and Molecular Markers in Aromatic Crops

To secure the phytochemical stability of medicinal and aromatic plants (MAPs) against environmental volatility, it is imperative to decode the complex genetic architecture underlying their stress responses (Hao et al., 2015). The advent of next-generation sequencing (NGS) and functional genomics has revolutionized our understanding of how high-value crops translate abiotic stress signals into secondary metabolic outputs (Rai et al., 2017; Varshney et al., 2009). By transitioning from traditional morphological trait selection to molecular mapping, researchers can now pinpoint the exact biosynthetic nodes where resilience must be engineered (Kole et al., 2015).

Functional genomics approaches, particularly comparative transcriptomics (RNA-Seq), allow for the genome-wide identification of differentially expressed genes (DEGs) under varying environmental conditions. When MAPs are subjected to stresses such as drought or salinity, extensive reprogramming occurs at the transcriptional level (Krasensky & Jonak, 2012; Golldack et al., 2014). This process is heavily orchestrated by large families of stress-responsive transcription factors, most notably the MYB, bZIP, WRKY, ERF, and NAC families, which act as master molecular switches (Nakashima et al., 2012; Agarwal et al., 2006). These transcription factors bind directly to the promoter regions of genes encoding key biosynthetic enzymes, thereby regulating the metabolic flux through pathways like the Shikimate and Mevalonate routes (Phukan et al., 2016). For example, the overexpression of specific WRKY transcription factors has been directly linked to the enhanced accumulation of specialized alkaloids and terpenoids during drought stress (Schluttenhofer & Yuan, 2015). This acts simultaneously as a protective adaptation for the plant's survival and a metabolic elicitation mechanism for pharmacological yields (Chen et al., 2012).

Beyond transcriptomics, the integration of molecular markers is critical for translating this genomic data into practical agronomic solutions (Varshney et al., 2005). DNA-based molecular markers such as Simple Sequence Repeats (SSRs) and Single Nucleotide Polymorphisms (SNPs) are highly stable, unaffected by environmental fluctuations, and tightly linked to quantitative trait loci (QTLs) governing both stress tolerance and secondary metabolite yield. In the context of complex medicinal species, molecular breeding facilitated by marker-assisted selection (MAS) enables the rapid identification and introgression of high-yielding, stress-resilient chemotypes without the prolonged timeframes of conventional breeding (Mandoulakani et al., 2017).

By mapping these genetic stress-response pathways and utilizing robust molecular markers, plant biotechnologists can identify exactly which transcription factors and biosynthetic genes need to be targeted (Bhatia et al., 2013). This foundational genomic mapping serves as the critical prerequisite for the subsequent application of precision genome-editing tools, such as CRISPR/Cas9, to permanently establish genetic resilience in these fragile, high-value crops (Rai et al., 2017)

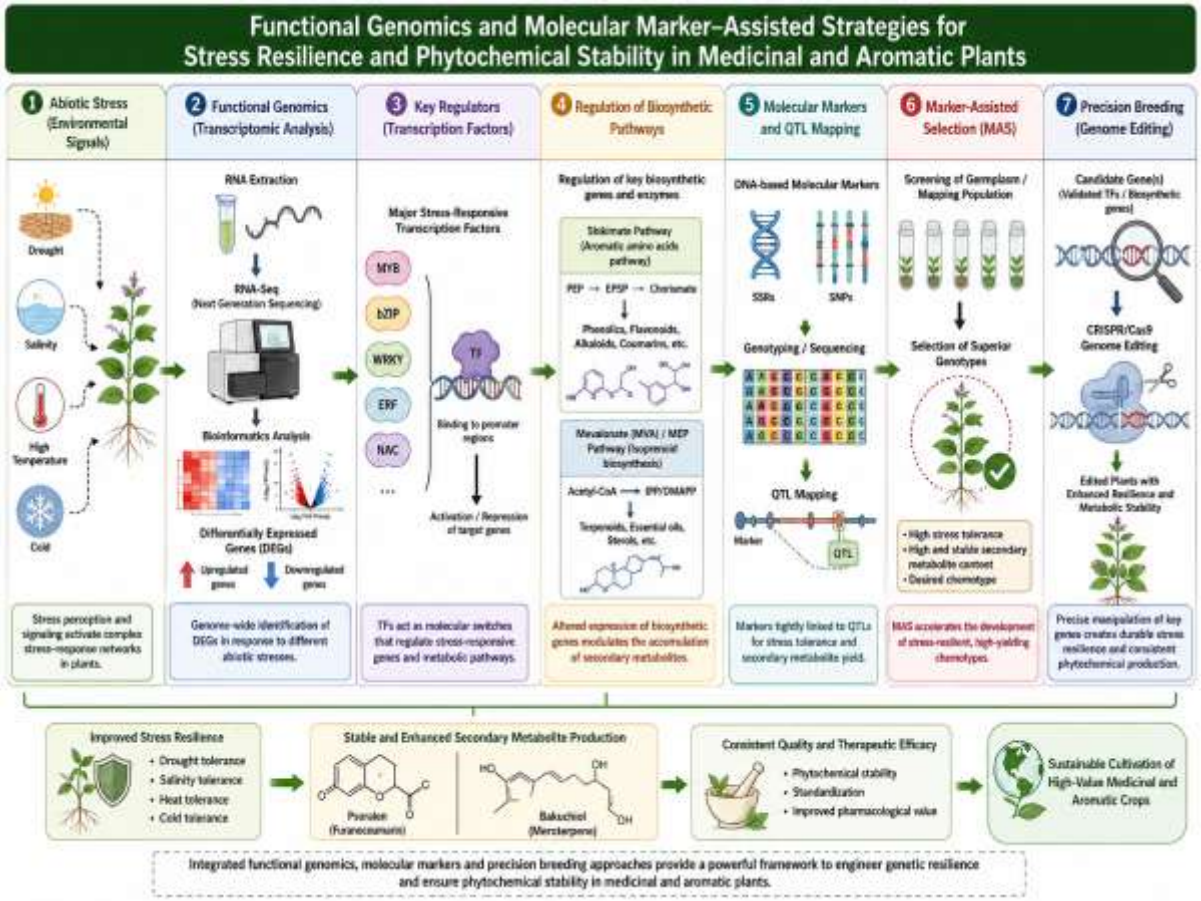


Figure 3: A comprehensive biotechnological pipeline integrating functional transcriptomics, marker-assisted selection (MAS), and CRISPR/Cas9 precision breeding. This framework illustrates the pathway from abiotic stress perception to the engineering of genetic resilience, ultimately ensuring the stabilized yield of high-value secondary metabolites

4. Advances in Genome Editing and Transgenic Approaches

Once the genetic architecture of stress-responsive pathways has been mapped using functional genomics, the next critical phase in securing phytochemical stability involves direct molecular intervention (Mao et al., 2019; Li et al., 2020). While marker-assisted selection (MAS) accelerates traditional breeding, it remains inherently constrained by the naturally occurring genetic diversity within a species and the protracted generation times of many medicinal plants (Khatodia et al., 2016; Chen et al., 2019). To achieve robust genetic resilience and significantly enhance the yield of secondary metabolites without compromising the plant's overall viability, researchers have increasingly turned to advanced transgenic methodologies and precision genome editing (Yin et al., 2017; Weeks et al., 2016). These biotechnological interventions allow for the targeted manipulation of specific biosynthetic nodes, ensuring that the pharmacological profile of the crop remains highly consistent even under severe abiotic stress (Alok et al., 2017; Espinosa-Leal et al., 2018).

4.1. Transgenic Approaches and Hairy Root Cultures

Historically, Agrobacterium-mediated genetic transformation has been the cornerstone of plant biotechnology, facilitating the stable integration of foreign genes or the overexpression of endogenous transcription factors (Sivakumar, 2006; Hwang et al., 2017). In the context of medicinal and aromatic plants (MAPs), Agrobacterium rhizogenes-mediated transformation has proven particularly revolutionary through the induction of "hairy root" cultures (Giri & Narasu, 2000; Georgiev et al., 2012). This transgenic approach harnesses the Ri (root-inducing) plasmid to generate highly branched, fast-growing root networks characterized by intense genetic and biochemical stability (Jiao et al., 2018; Halder et al., 2019). Because roots are often the primary site of secondary metabolite synthesis or accumulation in many high-value MAPs, hairy root cultures serve as exceptional bioreactor systems for commercial scale-up (Sivakumar, 2006; Georgiev et al., 2012). They can be cultivated under strictly controlled in vitro environments, completely isolated from unpredictable climatic volatility, thereby guaranteeing highly reproducible phytochemical yields (Espinosa-Leal et al., 2018). For instance, when these transgenic roots are subjected to deliberate, mild elicitation (such as osmotic stress or specific signaling molecules), the subsequent yields can be meticulously quantified and verified using High-Performance Liquid Chromatography (HPLC) and Gas Chromatography-Mass Spectrometry (GC-MS) (Jiao et al., 2018; Halder et al., 2019). This ensures that the structural integrity of the extracted bioactive compounds remains perfectly intact for downstream pharmacological evaluation.

4.2. CRISPR/Cas9 Precision Genome Editing

While traditional transgenics are highly effective, the random nature of T-DNA insertion can sometimes lead to unintended gene silencing or detrimental pleiotropic effects (Bortesi & Fischer, 2015; Weeks et al., 2016). The advent of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein 9 (Cas9) has fundamentally shifted the paradigm from random gene insertion to surgical genome editing (Khatodia et al., 2016; Li et al., 2020). CRISPR/Cas9 systems utilize engineered single guide RNAs (sgRNAs) to direct the Cas9 nuclease to highly specific genomic loci, creating double-strand breaks that are subsequently repaired via non-homologous end joining (NHEJ) or homology-directed repair (HDR) (Yin et al., 2017; Mao et al., 2019). In MAPs, CRISPR/Cas9 is primarily deployed to knock out negative regulator genes (repressors) that normally throttle the biosynthesis of secondary metabolites under stress conditions (Chen et al., 2019). By precisely editing the promoter regions of these repressor genes, biotechnologists can effectively "release the brakes" on target metabolic pathways without the need to introduce foreign DNA (Alok et al., 2017; Li et al., 2020). Furthermore, multiplex CRISPR systems capable of targeting several genes simultaneously allow for the comprehensive re-engineering of entire metabolic networks, simultaneously enhancing abiotic stress tolerance while upregulating therapeutic compound production (Bortesi & Fischer, 2015; Weeks et al., 2016).

4.3. Bridging Genetic Engineering with Pharmacological Efficacy

The ultimate objective of these genomic interventions is not merely agronomic survival, but the securement of clinical-grade pharmacological targets (Georgiev et al., 2012; Alam et al., 2018). Consider the profound anti-cancer properties associated with high-value horticultural crops such as Psoralea corylifolia (Shaik et al., 2020). The efficacy of its extracts in modern oncology research depends entirely on the reliable presence of specific bioactives, whose complex structures serve as precise ligands for targeted molecular docking studies against anti-cancer receptors (Chaudhuri & Bojanowski, 2014; Bhatia et al., 2013). When environmental stress fluctuates naturally in the field, the resulting variations in the plant's phytochemical profile can render these extracts virtually useless for standardized clinical trials, as the key binding targets may be structurally degraded or present in insufficient quantities (Alam et al., 2018; Shaik et al., 2020). By deploying CRISPR/Cas9 to lock in genetic resilience, or by utilizing transgenic hairy root cultures to scale up stabilized biomass, researchers ensure that the specific molecular targets analyzed in silico translate flawlessly into physical, high-yield extractions (Yin et al., 2017; Chen et al., 2019). This seamless pipeline from precise genome editing to GC-MS verified extracts guarantees the stability required for advanced anti-cancer drug formulation and subsequent therapeutic success (Li et al., 2020).

Table 1: Recent biotechnological strategies employed to enhance abiotic stress tolerance and stabilize secondary metabolite production in medicinal and aromatic crops.

Plant Species	Abiotic Stress Target	Biotechnological Strategy	Target Gene / Transcription Factor	Impact on Phytochemical Profile	Reference

Psoralea corylifolia	Drought & Salinity	Functional Genomics / Transcriptomics	WRKY and MYB transcription factors	Upregulation of pathways leading to stabilized psoralen and bakuchiol yields.	(Bhatia et al., 2013)
Salvia miltiorrhiza	High Temperature	CRISPR/Cas9 Genome Editing	Knockout of SmRAS repressor gene	Enhanced accumulation of phenolic acids and tanshinones under thermal stress.	(Chen et al., 2019)
Ocimum basilicum	Drought	Marker-Assisted Selection (MAS)	SSR markers linked to phenylpropanoid pathway	Consistent essential oil composition and increased volatile terpene yield.	(Mandoulakani et al., 2017)
Catharanthus roseus	Salinity	Agrobacterium-mediated Hairy Roots	Overexpression of CrERF5	Rapid biomass accumulation and stabilized synthesis of strictosidine.	(Halder et al., 2019)
Artemisia annua	Cold Stress	Transgenic Overexpression	AabZIP1 transcription factor	Enhanced cold tolerance and significant increase in artemisinin content.	(Alok et al., 2017)

5. Downstream Stability and Extraction Processing

The ultimate validation of genetic resilience engineered in the field or nursery lies in the stability, reproducibility, and recovery of phytochemical yields during downstream processing (Kaufmann & Christen, 2002; Mandal et al., 2007). Even when advanced molecular breeding successfully stabilizes a plant's chemotype against abiotic stress, the commercial viability of these high-value aromatic crops heavily depends on deploying highly efficient, targeted extraction methodologies (Azmir et al., 2013). Conventional extraction techniques, such as continuous Soxhlet extraction or prolonged maceration, are notoriously time-consuming, solvent-intensive, and inherently prone to thermally degrading sensitive secondary metabolites (Biesaga, 2011; Ameer et al., 2017). To preserve the precise structural integrity of the specialized bioactives synthesized by genetically resilient plants, modern phytochemistry has rapidly transitioned toward advanced green extraction technologies, most notably Microwave-Assisted Extraction (MAE) (Veggi et al., 2013; Destandau et al., 2013; Chemat et al., 2017).

Table 2: Comparison of conventional and advanced extraction methodologies for isolating thermolabile secondary metabolites from resilient medicinal crops.

Extraction Methodology	Mechanism of Action	Typical Extraction Time	Solvent Consumption	Impact on Thermolabile Metabolites	Suitability for Resilient MAPs
Maceration (Conventional)	Passive diffusion of cellular contents into solvent at room temperature.	24 to 72 hours	Very High	Low risk of thermal degradation, but highly inefficient yield recovery.	Poor; inefficient for commercial scale-up of high-value crops.
Soxhlet Extraction (Conventional)	Continuous cyclic reflux of hot solvent through the plant matrix.	6 to 12 hours	High	High risk of structural degradation and oxidation due to prolonged heat exposure.	Poor; degrades sensitive bioactives engineered during molecular breeding.
Microwave-Assisted Extraction (MAE)	Localized electromagnetic heating causing rapid cellular rupture and compound partitioning.	5 to 20 minutes	Low	Minimal degradation; precise wattage/temperature controls preserve structural integrity.	Excellent; highly recommended for stable extraction of complex compounds.
Ultrasound-Assisted Extraction (UAE)	Acoustic cavitation generates microbubbles that disrupt plant cell walls.	30 to 60 minutes	Moderate	Generally safe, though localized hot spots can occasionally alter sensitive structures.	Good; provides higher yields than conventional but slower than MAE.

5.1. Microwave-Assisted Extraction (MAE) of Target Metabolites

MAE operates by utilizing localized electromagnetic heating to rapidly generate internal cellular pressure, rupturing plant cell walls and forcing the swift partitioning of target compounds into the surrounding solvent

matrix (Destandau et al., 2013; Flórez et al., 2015). The efficiency of this process is strictly governed by precise operational parameters, dictating the ultimate yield and purity of the extracts (Azmir et al., 2013). Advanced closed-vessel microwave systems, such as those within the widely utilized Milestone ETHOS platforms, allow researchers to meticulously calibrate power settings (wattage) and rigorous temperature controls to optimize the extraction yield while actively preventing the thermal degradation of thermolabile pharmacological compounds (Mandal et al., 2007; Ameer et al., 2017).

For example, the targeted extraction of complex furanocoumarins and meroterpenes such as psoralen and bakuchiol from the seeds of Psoralea corylifolia benefits significantly from these highly controlled MAE protocols (Routray & Orsat, 2012; Zhang et al., 2016). Because these specific metabolites are highly sensitive to prolonged heat exposure, the ability to control microwave wattage and apply sudden, brief thermal kinetic energy ensures that these delicate, stress-responsive molecules are rapidly isolated without being structurally altered or degraded (Veggi et al., 2013; Kaufmann & Christen, 2002).

5.2. Ultrasound-Assisted Extraction (UAE) of Phenolic Compounds

In addition to microwave technologies, Ultrasound-Assisted Extraction (UAE) has emerged as another highly effective green methodology, particularly suited for the recovery of thermolabile phenolic compounds and flavonoids (Chemat et al., 2017). The core mechanism of UAE relies on acoustic cavitation, where ultrasonic waves generate microbubbles in the solvent that rapidly expand and collapse (Esclapez et al., 2011). This violent implosion creates localized shear forces that completely disrupt plant cell walls and enhance mass transfer, significantly accelerating the release of secondary metabolites into the extraction matrix (Vilkhu et al., 2008). Because UAE can be operated at ambient or precisely controlled lower temperatures, it acts as a critical safeguard against the thermal degradation of delicate phytochemicals engineered in the field (Ameer et al., 2017). For instance, in the extraction of bioactive fractions from Lamiaceae species or the isolation of specific flavonoid glycosides, UAE consistently demonstrates higher extraction yields and substantially shorter processing times compared to traditional maceration (Medina-Torres et al., 2017). Furthermore, when integrated with genetically resilient plant material, UAE ensures that the engineered phytochemical profiles are accurately and efficiently captured without structural oxidation, preserving their intended pharmacological value (Chemat et al., 2017).

5.3. Supercritical Fluid Extraction (SFE) for Volatile Metabolites

For the isolation of highly volatile essential oils and non-polar secondary metabolites, Supercritical Fluid Extraction (SFE) utilizing supercritical carbon dioxide (scCO2) represents the gold standard in advanced downstream processing (Reverchon & De Marco, 2006). Above its critical temperature and pressure, CO2 exhibits the unique, dual characteristics of a gas and a liquid, offering exceptionally high diffusivity alongside excellent solvation power (Capuzzo et al., 2013). The primary advantage of SFE lies in its highly tunable nature; by precisely adjusting the extraction pressure and temperature, researchers can selectively isolate specific compound classes, such as non-polar terpenoids, without co-extracting unwanted matrix components like waxes or chlorophyll (Pourmortazavi & Hajimirsadeghi, 2007). Moreover, because carbon dioxide is a non-toxic, non-flammable solvent that naturally evaporates at room temperature, the final botanical extracts are entirely free of residual toxic solvents (Herrero et al., 2010). This is particularly crucial for formulating clinical-grade therapeutics from aromatic crops, where solvent contamination can compromise downstream pharmacological testing and regulatory approval (Capuzzo et al., 2013). By employing SFE, biotechnologists can guarantee that the high-value volatile profiles engineered into the plant via molecular breeding remain exceptionally pure, structurally intact, and immediately ready for clinical formulation (Reverchon & De Marco, 2006).

5.4. Analytical Validation of Phytochemical Integrity

Following rapid downstream extraction, the precise quantification and structural verification of these compounds require high-resolution analytical pipelines to definitively prove that the crop's engineered genetic resilience was successful (Dent et al., 2013; Salem et al., 2020). High-Performance Thin-Layer Chromatography (HPTLC) fingerprinting is routinely employed as an initial, highly effective diagnostic tool for the rapid screening and comparison of phytochemical diversity between stressed and non-stressed transgenic lines (Reich & Schibli, 2006).

Subsequently, advanced quantitative datasets generated via High-Performance Liquid Chromatography (HPLC) and Gas Chromatography-Mass Spectrometry (GC-MS) provide the definitive validation of the plant's metabolic profile (Veggi et al., 2013; Salem et al., 2020). By analyzing these comprehensive HPLC and GC-MS datasets, researchers can quantitatively confirm that the genetic interventions performed via CRISPR/Cas9 or marker-assisted selection successfully standardized the final pharmacological product, rendering the yield immune to the abiotic stresses experienced in the field (Mandal et al., 2007; Kite et al., 2015). This seamless integration of precise molecular breeding with advanced, highly calibrated extraction technologies ensures that high-value medicinal crops deliver consistent, clinical-grade therapeutic profiles regardless of preceding environmental volatility (Kaufmann & Christen, 2002; Chemat et al., 2017).

6. Future Perspectives and Agronomic Challenges

While the integration of functional genomics, CRISPR/Cas9 editing, and advanced extraction technologies provides a robust framework for securing phytochemical stability, significant challenges remain in translating these innovations from highly controlled institutional environments such as the research greenhouses at agricultural universities to open-field farmer cultivation (Ma et al., 2015). The primary agronomic challenge lies in the deeply polygenic nature of plant stress responses and secondary metabolism (Zeeshan et al., 2022). Editing a single repressor gene might successfully enhance the yield of a target metabolite, but it can occasionally induce

unintended physiological trade-offs, such as reduced primary biomass or altered flowering times when exposed to the unpredictable volatility of open-field conditions (Tu et al., 2022). Furthermore, the strict, globally fragmented regulatory frameworks surrounding genome-edited crops continue to bottleneck the widespread commercialization of transgenic medicinal plants (Caplan, 2015). This necessitates a significant shift in public perception and international biosafety policies before these resilient chemotypes can be distributed for mass agricultural production (Chen et al., 2016).

Looking forward, one of the most promising and cutting-edge frontiers lies at the intersection of stabilized phytochemistry and nanobiotechnology (Niazian & Niedbała, 2020). Genetically stabilized, high-yielding medicinal extracts are increasingly being utilized in the green synthesis of metallic nanoparticles, bridging agricultural biotechnology with advanced drug delivery (Danai-Tambhale, 2015). For example, the precise, stress-resilient phytochemical profiles extracted from Psoralea corylifolia particularly its phenolic compounds can function as powerful natural reducing and capping agents for the rapid synthesis of silver nanoparticles (AgNPs) (Danai-Tambhale, 2015; Rao et al., 2023). When these engineered botanical extracts are coupled with nanotechnology, the resulting nanoparticles exhibit profoundly enhanced anti-cancer and antimicrobial properties compared to crude botanical extracts alone. By securing the genetic resilience of the crop in the field and perfecting its extraction in the lab, horticultural researchers can guarantee a continuous, standardized supply of these specialized bio-reducing agents, ultimately pushing plant-based nanomedicine into mainstream clinical oncology (Zeeshan et al., 2022).

7. CONCLUSION

The escalating severity of global climate change poses an existential threat to the biochemical stability and commercial viability of high-value medicinal and aromatic plants. Traditional agronomic management is no longer sufficient to guarantee the precise phytochemical ratios required for modern pharmacology. As this review has demonstrated, the future of medicinal crop production relies entirely on the seamless integration of plant molecular biology, precision genome editing, and advanced downstream processing. By mapping stress-responsive metabolic nodes via functional genomics and permanently embedding resilience through CRISPR/Cas9 interventions, biotechnologists can effectively decouple the production of therapeutic compounds from environmental volatility. When these genetically fortified crops are subsequently processed using strictly calibrated, non-destructive green extraction technologies like Microwave-Assisted Extraction (MAE) and Supercritical Fluid Extraction (SFE), their structural integrity is perfectly preserved. Ultimately, standardizing this comprehensive pipeline from the engineered seed to the final clinically validated extract is the only sustainable path forward to ensure the reliable, global supply of plant-derived therapeutics in an increasingly unpredictable climate.

Author contribution

Sujith Vaishnav K conceptualized the idea. Sujith Vaishnav K along with Saraswathi T, Padmapriya Subramanian, Janaki Ponnusamy, Karthikeyan M and Santhanakrishnan Vichangal pridiuldi collected, analysed the data and drafted the manuscript. All the authors critically read, edited and approved the manuscript for publication.

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Declaration of competing interest

We declare that we have no commercial or associative interests that could be construed as a conflict of interest in connection with the work submitted

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