

CHAPTER 5

Phytotherapy against amino acid disorders

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Abstract

Amino acid disorders, including aminoacidopathies and urea cycle defects, pose significant clinical challenges due to toxic metabolite accumulation and limited therapeutic options. Phytotherapy offers a promising complementary approach through plant-derived metabolites capable of modulating metabolic pathways, enhancing enzymatic activity and reducing oxidative and inflammatory stress. Present study highlighted key medicinal plants traditionally employed against disorders and their mechanisms such as phenylalanine, leucine, methionine and organic acid metabolism defects. The recent work reviews current evidence on species including *Andrographis paniculata*, *Asparagus officinalis*, *Curcuma longa* and *Phyllanthus emblica*, providing an updated perspective on the therapeutic potential of phytochemicals in managing amino acid disorders and outlining avenues for future research.

Keywords: Aminoacidopathies, clinical challenges, metabolite accumulation, therapeutic potential

Introduction

Amino acid metabolism disorders are inherited enzymatic defects that disrupt normal amino acid processing, including aminoacidopathies, organic acidemias and urea cycle defects (Vliet *et al.*, 2011; Odukoya *et al.*, 2021). These disruptions lead to the accumulation of toxic intermediates or the deficiency of essential metabolic products, resulting in neurological impairments, developmental delays, metabolic crises and multi-organ dysfunction (Biswas *et al.*, 2021; Ijaz *et al.*, 2025). Conventional management strategies primarily rely on strict dietary control, enzyme replacement, cofactor supplementation and in severe cases, organ transplantation. However, these approaches often offer only partial relief, may carry adverse effects and remain inaccessible in many regions (Dattilo *et al.*, 2016; Berger *et al.*, 2022). Growing scientific interest in recent years has focused on phytotherapy as a complementary or supportive strategy in metabolic disorders (Abdulghani and Al-Fayyadh, 2024). Medicinal

plants contain a wide spectrum of bioactive compounds (El-Saadony *et al.*, 2025). These phytochemicals have demonstrated potential in mitigating metabolic imbalances, reducing oxidative stress associated with toxic metabolite buildup and enhancing the cellular resilience (Jena *et al.*, 2025). Traditional medicinal systems across various cultures have long utilized plants for symptoms now understood to be associated with metabolic dysfunction (Manisha *et al.*, 2025; Ofoezie *et al.*, 2025). Modern research is beginning to validate these applications, identifying species such as *Andrographis paniculata*, *Asparagus officinalis*, *Curcuma longa* and *Phyllanthus emblica* as promising candidates for managing amino acid related disorders (Wu *et al.*, 2023; Mukherjee and Singh, 2025). Despite these advances, the therapeutic role of phytotherapy remains underexplored and warrants systematic scientific evaluation. The present study provides a comprehensive overview of medicinal plants reported to exhibit beneficial effects against specific amino acid disorders. By integrating traditional knowledge with emerging experimental evidence, present documentation aims to highlight the potential of plant-based interventions as adjunct strategies in the management of these complex genetic conditions and to stimulate future research in this evolving field.

Methodology

A detailed assessment of the available literature has been carried out on the medicinal plants that have been traditionally used by the common people. Keywords including "ethnomedicinal plants", "herbal remedies", "traditional practices", "pharmacological potential", "medicinal uses", "mode of administration" and "natural healthcare practices" were used to search a variety of databases, including PubMed, Scopus, Web of Science, NCBI and others. To learn more about the ethnomedicinal plants used to treat amino acid problems, pertinent books and papers were reviewed. Following the author's identification of the plant species, floral books were consulted (Islam *et al.*, 2025; Kumar, 2025).

Results and discussion

The present analysis highlighted the potential role of phytotherapy in the management of selected amino acid metabolism disorders. A total of eight amino acid related metabolic disorders were identified, each associated with a specific medicinal plant reported in the literature to exert supportive or modulatory effects on the underlying biochemical dysfunctions (Table 1; Figure 1). The disorders included enzymatic deficiencies affecting amino acid synthesis, degradation, and detoxification pathways, such as asparagine synthetase deficiency, phenylalanine hydroxylase deficiency, homocystinuria, maple syrup urine disease (MSUD), methylmalonic acidemia, ornithine transcarbamylase (OTC) deficiency, phosphoglycerate dehydrogenase deficiency and urea cycle disorders (UCDs). Medicinal plants identified in relation to these disorders belonged to diverse botanical families and included *Phyllanthus emblica*, *Vicia faba*, *Allium sativum*, *Cucurbita moschata*, *Asparagus officinalis*, *Andrographis paniculata*, *Glycine max* and *Curcuma longa*. These plants are known to possess bioactive compounds such as polyphenols, flavonoids, sulfur-containing compounds, vitamins and alkaloids, which may influence metabolic homeostasis. The reported mechanisms of action were largely indirect, focusing on antioxidant activity, hepatoprotection, enhancement of mitochondrial function and modulation of nitrogen metabolism. Several plants demonstrated relevance in disorders associated with

hyperammonemia, oxidative stress or impaired amino acid biosynthesis, suggesting a common phytotherapeutic pattern targeting metabolic stress rather than direct enzyme replacement. Amino acid metabolism disorders are primarily genetic and enzyme-specific in nature; therefore, conventional management relies on dietary restriction, supplementation and pharmacological interventions. However, present findings summarized in this study suggested that phytotherapy may serve as a complementary strategy by alleviating secondary metabolic complications associated with these disorders. *Phyllanthus emblica*, identified in asparagine synthetase deficiency, is rich in antioxidants that may support neuronal and cellular metabolism under conditions of impaired amino acid synthesis (Singh *et al.*, 2018). Similarly, *Glycine max* may help compensate for reduced serine biosynthesis in phosphoglycerate dehydrogenase deficiency by providing exogenous amino acids and metabolic cofactors (Torres *et al.*, 2006). *Allium sativum* contains sulfur-containing compounds that are known to influence homocysteine metabolism, potentially reducing cardiovascular and neurological complications (Norbert *et al.*, 2006). Likewise, *Cucurbita moschata* may mitigate oxidative stress linked to branched-chain amino acid accumulation in MSUD (Islam *et al.*, 2025). These plants may enhance hepatic detoxification capacity and reduce ammonia-induced neurotoxicity, thereby supporting metabolic balance. Present results indicated that medicinal plants do not act as direct substitutes for deficient enzymes but rather exert supportive, protective and modulatory effects that may improve patient outcomes when used alongside standard therapies.

Table 1: List of medicinal plants could be used against amino acid disorders and their mechanisms

Amino acid disorders	Plants can be used against the disorder & mechanism	Sources
Asparagine synthetase deficiency (Insufficient production of asparagine)	<i>Phyllanthus emblica</i> L.	Singh <i>et al.</i> , (2018)
Benign hyperphenylalaninemia (deficiency of phenylalanine hydroxylase)	<i>Vicia faba</i> L.	Ahmed <i>et al.</i> , (2022)
Homocystinuria (Inability to process homocysteine)	<i>Allium sativum</i> L.	Norbert <i>et al.</i> , (2006)
Maple syrup urine disease (MSUD) (prevents breakdown of amino acids like leucine, isoleucine and valine)	<i>Cucurbita moschata</i> Duchesne	Islam <i>et al.</i> , (2025)
Methylmalonic acidemia (Inability to metabolize fats and amino acids)	<i>Asparagus officinalis</i> L.	Olas, (2024)

Ornithine transcarbamylase (OTC) deficiency (Build toxic ammonia; hyperammonemia)	<i>Andrographis paniculata</i> (Burm.f.) Wall. ex Nees	Mukherjee and Singh, (2025)
Phosphoglycerate dehydrogenase deficiency (Inability of serine production)	<i>Glycine max</i> (L.) Merr.	Torres <i>et al.</i> , (2006)
Urea cycle disorders (UCDS) (Unable to remove toxic ammonia from protein breakdown)	<i>Curcuma longa</i> L.	Wu <i>et al.</i> , (2023)

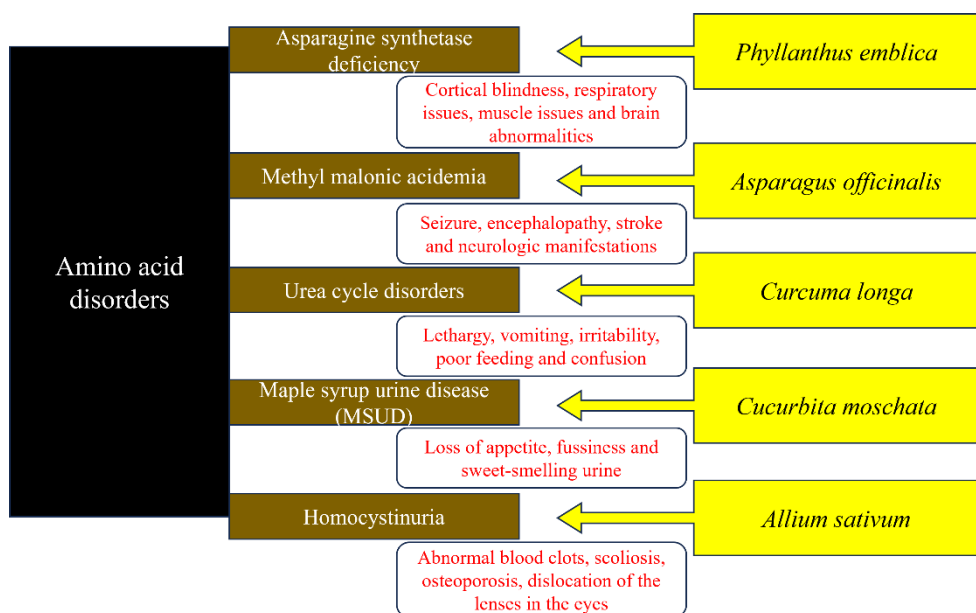


Figure 1: Different amino acid disorders with their relevant symptoms which can be treated by common ethnomedicinal plants

Biotechnological approaches

Plant tissue culture and micropropagation techniques, which enable the sustainable production of medicinal plants listed in Table 1. Advancements in metabolic engineering and genetic transformation further enable targeted manipulation of biosynthetic pathways to increase the production of specific metabolites of therapeutic interest. Modern biotechnology can also incorporate omics-based platforms including genomics, transcriptomics, proteomics and metabolomics to identify active compounds and elucidate molecular mechanisms underlying their effects on amino acid metabolic pathways. Metabolomic profiling, for

instance, can help characterize compounds involved in reducing oxidative stress or supporting hepatocellular detoxification in conditions such as methylmalonic acidemia and urea cycle disorders (Wu *et al.*, 2023; Olas 2024).

Conclusion

Amino acid metabolism disorders present significant clinical challenges due to their genetic origin, complex biochemical disturbances and the limited effectiveness of current therapeutic options. Present findings of the study highlighted the potential value of phytotherapy as a supportive approach in managing these conditions. Most reports are preliminary, emphasizing the need for systematic experimental studies and well-designed clinical trials to validate efficacy, determine optimal dosages and ensure safety. Nonetheless, the integration of traditional knowledge with modern biochemical understanding provides a valuable foundation for future research. Continued investigation into plant-based therapeutics could contribute to the development of sustainable healthcare formulations.

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