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Integrated nutrient management and physiological responses in Kalmegh (*Andrographis paniculata*): A comprehensive review

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Abstract
Integrated nutrient management (INM) is a key approach for maintaining soil fertility, increasing crop productivity, and promoting environmental safety in medicinal plant cultivation. Kalmegh (*Andrographis paniculata* Burm. f. Wall. ex Nees), a medicinal herb valued for its bioactive compound andrographolide, demonstrates marked physiological sensitivity to soil nutrient availability. This review synthesizes research from global and Indian contexts regarding the effects of organic manures, inorganic fertilizers, and biofertilizers, both individually and in combination, on the growth, yield, nutrient uptake, quality, and economic outcomes of Kalmegh cultivation. The combined application of organic and inorganic nutrient sources significantly increases plant height, leaf area, branching, and biomass by enhancing photosynthetic activity and root development. The use of farmyard manure, vermicompost, and balanced nitrogen, phosphorus, and potassium (NPK) fertilization improves the rhizosphere environment by enhancing soil physicochemical and biological properties, nutrient-use efficiency, and microbial enzymatic activity. Physiological studies reveal that organic-inorganic integration enhances chlorophyll content, stomatal conductance, and nutrient assimilation, resulting in greater accumulation of andrographolide and other secondary metabolites. Biofertilizers, including *Azospirillum, Azotobacter, Trichoderma harzianum*, and *vesicular-arbuscular mycorrhiza* (VAM), further enhance phosphorus uptake and influence hormonal and enzymatic processes related to plant growth and stress tolerance. Economic analyses consistently demonstrate higher net returns and benefit-cost ratios for integrated nutrient management compared to the exclusive use of either organic or inorganic inputs. This review highlights the diverse physiological mechanisms and sustainability advantages of integrated nutrient management in Kalmegh cultivation. INM contributes to maintaining soil health, maximizing herbage yield, and improving phytochemical quality. Future research should prioritize standardizing nutrient combinations, investigating microbial consortia, and incorporating nanofertilizers and precision nutrient management technologies to support sustainable and high-quality production of *Andrographis paniculata*.

Keywords: Kalmegh, INM, organic manure, andrographolide, biofertilizers, sustainable soil fertility, physiological response

1. Introduction

Kalmegh (*Andrographis paniculata* Burm. f. Wall. ex Nees), belonging to the family Acanthaceae, is an annual medicinal herb extensively cultivated across tropical Asia, particularly in India, Sri Lanka, Thailand, and China. Popularly known as the "King of Bitters," it is one of the most commercially significant medicinal plants owing to its principal bioactive compound, andrographolide a diterpenoid lactone with proven hepatoprotective, antiviral, antioxidant, anti-inflammatory, and immunomodulatory activities (Mishra and Jain, 2013; Verma *et al*., 2015) [15, 35]. The global surge in the demand for herbal medicines and nutraceuticals has greatly enhanced the economic relevance of Kalmegh in both pharmaceutical and phytochemical industries.

Over the past century, the intensification of agricultural systems has substantially improved crop yields but also led to soil degradation, nutrient imbalances, and environmental stress, primarily due to excessive reliance on chemical fertilizers. To address these challenges, Integrated Nutrient Management (INM) has emerged as a sustainable strategy to maintain productivity while preserving soil health. INM emphasizes the balanced use of organic, inorganic, and biological nutrient sources to synchronize nutrient availability with crop demand, enhance nutrient-use efficiency, and minimize environmental.

Organic amendments such as farmyard manure (FYM), vermicompost, green manures, and biofertilizers improve soil physical structure, microbial activity, and nutrient retention capacity, whereas inorganic fertilizers provide readily available nutrients for immediate plant uptake. The integrated use of these sources sustains long-term soil fertility and ensures balanced nutrient supply throughout the crop cycle. In *A. paniculata*, nutrient management profoundly influences herbage yield and the biosynthesis of secondary metabolites, especially andrographolide. Given its extensive leaf biomass and high photosynthetic rate, the crop is highly responsive to balanced nutrient application, particularly nitrogen, phosphorus, potassium, and micronutrients (Tiwari *et al*., 2012) [32].

Macronutrients and micronutrients perform distinct yet synergistic roles in the physiological and biochemical functions of Kalmegh. Nitrogen promotes chlorophyll synthesis, amino acid formation, and vegetative growth; phosphorus enhances root proliferation and energy transfer; potassium regulates enzyme activation, osmotic balance, and secondary metabolite synthesis; while micronutrients such as Zn, Fe, Mn, and Cu act as cofactors in enzymatic and redox reactions. The combined use of organic and inorganic nutrient sources creates a favorable *rhizospheric* environment by stimulating microbial biomass, enhancing soil enzymatic activities, and facilitating nutrient solubilization. Furthermore, biofertilizers like *Azospirillum*, *Azotobacter*, *Trichoderma harzianum*, and *vesicular arbuscular mycorrhiza* (VAM) enhance nutrient uptake and plant vigor by improving root colonization, hormonal signalling, and photosynthetic efficiency (Aparna and Bagyaraj, 2007; Sanjutha *et al*., 2008) [3, 27].

Sustainable cultivation of medicinal plants such as Kalmegh requires nutrient management practices that maintain ecological integrity while ensuring high productivity and phytochemical quality. Continuous dependence on synthetic fertilizers can reduce soil organic matter, suppress microbial diversity, and negatively impact the biosynthesis of secondary metabolites responsible for therapeutic efficacy. Conversely, INM approaches recycling organic residues, reduces dependence on chemical inputs, and promotes a resilient soil microbiome. The slow nutrient release from organic sources complements the rapid availability from mineral fertilizers, ensuring continuous nutrient supply throughout the plant's growth stages (Hemalatha and Suresh, 2012) [12].

Recent studies have demonstrated that integrating FYM, compost, and biofertilizers with balanced NPK fertilization significantly enhances plant growth, herbage yield, andrographolide concentration, and economic returns in *A. paniculata* across diverse agro-ecological conditions. Importantly, such integrative nutrient approaches align with the principles of Good Agricultural and Collection Practices (GACP) for medicinal plants, ensuring sustainable production and consistent quality standards essential for the herbal pharmaceutical sector.

Therefore, this review aims to synthesize and critically evaluate current research on nutrient management strategies in *Andrographis paniculata*, with a particular focus on their influence on growth, yield, soil fertility, and secondary metabolite production.

2. Effect of Organic and Inorganic Nutrient Management on Growth Attributes

2.1 Physiological Perspective on Growth Response

Plant growth reflects complex physiological and biochemical processes shaped by nutrient availability. In *Andrographis paniculata*, traits such as plant height, leaf number, branching, and biomass depend on balanced nutrition. Nitrogen supports chlorophyll and protein synthesis; Phosphorus participates in ATP synthesis, and potassium regulates enzyme activity and photosynthate movement. Integrating organic manures with inorganic fertilizers ensures a balanced, sustained nutrient supply, promoting root growth, microbial activity, and overall physiological efficiency (Muniramappa *et al*., 1997; Sanjutha *et al*., 2008) [16, 27].

2.2 Influence of Nitrogen and Phosphorus Fertilization

Nitrogen and phosphorus are pivotal macronutrients governing vegetative growth and canopy development in *Andrographis paniculata*. Muniramappa *et al*. (1997) [16] reported that the application of 100:75 kg ha^{-1} N and P significantly enhanced plant height, canopy spread, branching, and leaf area, primarily through improved chlorophyll synthesis and root development. Similarly, Tiwari *et al*. (2012) [32] observed that 60 kg N ha^{-1} applied through farmyard manure promoted greater plant height, leaf number, and branch proliferation. These findings collectively demonstrate that balanced N and P fertilization enhances photosynthetic surface area, accelerates cellular differentiation, and contributes to higher biomass accumulation.

2.3 Impact of Organic Manures on Vegetative Growth

Organic manures enhance plant growth by supplying nutrients and improving soil physical and biological properties. Mannikeri (2006) [14] reported that vermicompost at 15.56 t ha^{-1} maximized plant height, leaf number, and leaf area index in turmeric, demonstrating the role of organic carbon in promoting vegetative vigour, principles applicable to *Andrographis paniculata*. Similarly, Rajamani *et al*. (2007) [22] and Sanwal *et al*. (2007) [28] observed that the combined application of FYM and vermicompost increased leaf area and leaf number by improving microbial activity and soil moisture retention. In Kalmegh, Ram *et al*. (2008) [23] found that FYM enhanced plant spread and leaf production, while Sanjutha *et al*. (2008) [27] reported that integrating FYM (15 t ha^{-1}) with NPK (75:75:50 kg ha^{-1}) and Panchagavya (3%) foliar spray produced maximum plant height and branching, indicating improved nutrient translocation and biomass accumulation.

2.4 Effects of Biofertilizers and Mycorrhizal Inoculants

Microbial inoculants play a crucial role in nutrient solubilization, nitrogen fixation, and hormonal regulation. Aparna and Bagyaraj (2007) [3] reported that inoculation of *Andrographis paniculata* with Glomus mosseae and *Trichoderma harzianum* enhanced plant growth, biomass yield, and phosphorus uptake while reducing phosphatic fertilizer requirements by 25%. These benefits were attributed to improved phosphorus solubilization, greater root surface area, and stimulation of plant growth-promoting *rhizobacteria* (PGPR).

The contribution of *arbuscular mycorrhizal fungi* (AMF) to enhanced phosphorus and water uptake underscores the importance of biofertilizer-nutrient integration in sustainable cultivation systems. Similarly, Velmurugan *et al*. (2008) [34] found in turmeric that the combined application of FYM (30 t ha⁻¹), *Azospirillum*, Phosphobacteria, and VAM significantly increased plant height and leaf number. Such synergistic interactions between organic amendments and microbial inoculants enhance enzymatic activities like phosphatase and dehydrogenase, promoting efficient nutrient cycling and sustained nutrient availability in Kalmegh.

2.5 Role of Vermicompost and Organic Residues

Vermicompost, rich in humic substances, growth regulators, and readily available nutrients, enhances root development, chlorophyll synthesis, and enzymatic activity. Vijaya *et al*. (2008) [36] reported that coir-pith-based vermicompost improved *Andrographis paniculata* growth even in alkaline soils, while Zafar and Shweta (2010) [37] observed similar benefits using cow dung-based vermicompost under partial shade. Sharma (2016) [30] further demonstrated that vermicompost at 7.5 t ha^{-1} significantly increased plant height, leaf number, and branching compared with lower doses. These improvements are attributed to slow nutrient release, bioactive compounds, and enhanced cytokinin-mediated leaf initiation and carbon assimilation.

2.6 Integration of Organic and Inorganic Sources for Growth Optimization

The combined use of organic and inorganic fertilizers ensures nutrient synchronization organics enhance nutrient retention, while mineral fertilizers provide rapid availability. Ramesh *et al*. (2011) [25] reported that integrated fertilization improved growth attributes in *Andrographis paniculata*. Hemalatha and Suresh (2012) [12] found that FYM (15 t ha^{-1}) + NPK (45:25:25 kg ha^{-1}) + *Azospirillum* (1 kg ha^{-1}) produced maximum plant height, branching, and leaf area. Similarly, Mishra and Jain (2013) [15] observed that *biofertilizers* (*Azotobacter* + PSB) with 50% RDF and 5 t ha^{-1} vermicompost yielded the highest growth performance, while Goel and Duhan (2013) attributed growth improvement under FYM (12.5 t ha^{-1}) to enhanced soil organic carbon and nutrient exchange efficiency.

2.7 Comparative Efficiency of Different Organic Sources

The efficiency of organic sources depends on their nutrient composition and decomposition rate. Detpiratmongkol *et al*. (2014) [10] reported that chicken manure at 12.5 t ha^{-1} produced greater plant height, stem and leaf dry weight, and leaf area index than cow or pig manure due to higher N and P content and faster mineralization. Similarly, Chumthong and Detpiratmongkol (2016) [8] found that increasing chicken manure rates enhanced biomass in *Stevia rebaudiana*, highlighting the effectiveness of organic nitrogen in medicinal crops.

In *Andrographis paniculata*, Patel *et al*. (2016) [19] recorded maximum height and branching with 100% recommended nitrogen through neem cake, while Sharma (2016) [30] reported enhanced growth with vermicompost integration. Overall, integrated nutrient management (INM) improves vegetative growth in Kalmegh by enhancing soil health, microbial activity, and nutrient uptake. The synchronized nutrient release from organic and inorganic sources results in higher chlorophyll content, larger leaf area, and vigorous branching, thereby increasing photosynthetic efficiency and biomassa accumulation.

2.2 Effect of Integrated Nutrient Management on Yield Attributes and Yield

2.2.1 Physiological Basis of Higher Yield in Kalmegh

Yield in *Andrographis paniculata* results from coordinated morpho-physiological processes such as photosynthesis, assimilate partitioning, nutrient translocation, and secondary metabolite synthesis. Herbage yield, expressed as fresh or dry biomass, depends on vegetative vigor and the duration of active photosynthesis. Organic manures enhance soil organic matter, microbial biomass, and nutrient mineralization, while inorganic fertilizers ensure timely macronutrient availability. Their integrated use sustains nutrient supply, extends canopy activity, and improves assimilate conversion efficiency, thereby enhancing biomass and andrographolide yield (Hemalatha and Suresh, 2012; Tiwari *et al*., 2012) [12, 32].

2.2.3 Impact of Organic Manures on Biomass and Foliage Yield

The beneficial effects of organic manures on the yield attributes of medicinal and aromatic crops are well established. At the National Research Centre for Medicinal and Aromatic Plants, Boriavi (Anand, Gujarat), FYM at 15 t ha^{-1} significantly increased the fresh and dry root yield of *Chlorophytum borivilianum* (Anonymous, 2001) [2], suggesting similar potential in *Andrographis paniculata* under comparable conditions.

FYM enhances cation exchange capacity, microbial activity, and nutrient uptake efficiency, thereby improving carbon assimilation. Patel *et al*. (2008) [23] also reported maximum root yield in *Safed Musli* with poultry manure (5 t ha^{-1}) and FYM (10-20 t ha^{-1}). In *A. paniculata*, Ram *et al*. (2008) [23] and Sanjutha *et al*. (2008) [27] found that FYM (15 t ha^{-1}) + NPK (75:75:50 kg ha^{-1}) + Panchagavya (3%) foliar spray produced the highest herbage yield through improved leaf area, biomass accumulation, and sustained photosynthetic activity, highlighting the synergistic benefits of integrated nutrient management.

2.2.4 Integrated Nutrient Management Enhancing Herbage Yield

Integrated Nutrient Management (INM) promotes nutrient synchronization, optimizing uptake during peak growth stages of *Andrographis paniculata*. Ramesh *et al*. (2011) [25] reported that combined organic and inorganic fertilization produced the highest foliage biomass and dry matter yield. The inclusion of biofertilizers enhanced microbial activity, nutrient availability, and nutrient-use efficiency. Hemalatha and Suresh (2012) [12] achieved maximum fresh (1.392 t ha^{-1}) and dry foliage yield (2.639 t ha^{-1}) with FYM (15 t ha^{-1}) + NPK (45:25:25 kg ha^{-1}) + *Azospirillum* (1 kg ha^{-1}). Similarly, Tiwari *et al*. (2012) [32] observed that 60 kg N ha^{-1} applied through FYM produced maximum fresh (37.12 q ha^{-1}) and dry yield (25.59 q ha^{-1}). The enhanced yield under integrated treatments was attributed to improved nutrient uptake, root colonization, and extended photosynthetic duration, resulting in higher carbon assimilation and biomass production.

2.2.5 Effect of Biofertilizers and Organic-Inorganic Synergy

Biofertilizers improve yield by facilitating nitrogen fixation, phosphate solubilization, and phytohormone production. Aparna and Bagyaraj (2007) [3] found that inoculation with *Glomus mosseae* and *Trichoderma harzianum* enhanced biomass yield and phosphorus uptake, reducing P fertilizer requirements by 25%. Chaudhari *et al*. (2013) [5] reported higher dry foliage yield with FYM (7.5 t ha^{-1}), while Shahjahan *et al*. (2013) [29] observed that vermicompost application increased total dry matter yield (6.6 t ha^{-1}) compared with control (3.0 t ha^{-1}). The presence of humic substances and growth regulators in vermicompost enhanced nutrient mineralization, enzymatic activity, and assimilate partitioning, contributing to higher yield performance.

2.2.6 Comparative Role of Different Organic Sources

The effectiveness of organic manures depends on nutrient composition and mineralization rate. Detpiratmongkol *et al*. (2014) [10] reported that chicken manure (12.5 t ha^{-1}) produced higher plant height, total dry weight, and leaf area index than cow or pig manure due to its higher N content and faster decomposition. Khan *et al*. (2015) found that vermicompost combined with *Azotobacter chroococcum* improved the leaf-to-stem ratio and fresh foliage yield in Kalmegh. Enhanced nitrogen assimilation and root efficiency under such treatments supported continuous nutrient uptake and biomass production. Organic manures also enriched the rhizosphere microbial community and increased enzymatic activities (urease, dehydrogenase, phosphatase), ensuring sustained nutrient cycling.

2.2.7 Response to Inorganic Fertilization and Its Integration

Andrographis paniculata responds positively to balanced inorganic fertilization, particularly when integrated with organics. Chauhan and Tiwari (2003) [32] reported maximum dry foliage yield (2185.19 kg ha^{-1}) with 40 kg N ha^{-1} through urea, compared to 1601.85 kg ha^{-1} in the control, indicating nitrogen's pivotal role in promoting vegetative growth and chlorophyll synthesis. Integration with organics improved fertilizer efficiency by reducing nutrient losses and enhancing retention. Dakhane and Nandkar (2012) [9] demonstrated that balanced application of macro- and micronutrients (N, P, K, Ca, Mg, Fe, Mn, Zn, Cu) yielded the highest dry foliage biomass, underscoring the importance of secondary and micronutrients in enhancing photosynthetic efficiency and metabolic activity.

2.2.8 Integrated Nutrient Management Enhancing Andrographolide Yield

Andrographolide yield is governed by both total biomass and its concentration in plant tissue. INM practices that maximize vegetative growth concurrently enhance andrographolide accumulation through improved nitrogen assimilation and secondary metabolism. Prabhu *et al*. (2009) [21] reported that foliar application of 2% Panchagavya + 0.2% humic acid + 2% moringa leaf extract yielded 1956 kg dry herbage ha^{-1} with a benefit-cost ratio of 2.47. Such integrative treatments improve photosynthetic activity and activate metabolic pathways associated with secondary metabolite biosynthesis, offering simultaneous gains in yield and phytochemical quality.

2.2.9 Physiological Interpretation and Yield Determinants

The yield responses under integrated nutrient management can be attributed to the following physiological mechanisms:

- **Enhanced Leaf Area Duration (LAD):** INM promotes sustained leaf expansion and chlorophyll content, prolonging the photosynthetically active period.
- **Improved Nutrient Assimilation:** Organic-inorganic synergy increases the availability and uptake of macro- and micronutrients essential for carbon and nitrogen metabolism.
- **Increased Translocation Efficiency:** Balanced nutrition enhances the conversion of photosynthates into biomass and active compounds.
- **Soil Microbial Synergy:** Organic matter promotes microbial biomass and enzyme activity, aiding nutrient cycling and stress resilience.
- **Hormonal Modulation:** Bio fertilizers and organic amendments stimulate auxin and cytokinin production, promoting branching and biomass accumulation.
- These combined effects lead to higher fresh and dry herbage yields, improved leaf-to-stem ratio, and enhanced secondary metabolite synthesis, confirming that INM is superior to either organic or inorganic fertilization alone.

2.1.3 Effect of Integrated Nutrient Management on Nutrient Uptake and Availability

Physiological Basis of Nutrient Uptake in Kalmegh

Efficient nutrient uptake and utilization are fundamental to the productivity and phytochemical quality of *Andrographis paniculata*. Uptake involves root growth, ion transport, and assimilation processes influenced by soil fertility and rhizospheric activity. Integrated Nutrient Management (INM) enhances these processes by improving root morphology, microbial activity, and nutrient availability, ensuring a sustained supply throughout the crop cycle. Nitrogen and phosphorus support chloroplast development and metabolic synthesis, while potassium regulates enzyme activity and osmotic balance. Organic matter further enhances cation exchange capacity (CEC), pH buffering, and microbial-mediated nutrient solubilization, resulting in synchronized nutrient release and improved uptake efficiency (Aparna and Bagyaraj, 2007; Verma *et al*., 2015) [3, 35].

Differential Uptake Patterns among Kalmegh Species

Alagesaboopathi and Balu (1995) [1] reported significant interspecific variation in nutrient accumulation among *Andrographis* species. *A. alata* showed the highest leaf magnesium, *A. paniculata* the highest potassium, and *A. lineata* the highest manganese and iron content. These differences reflect species-specific genetic potential and root physiology, emphasizing the importance of maintaining balanced soil nutrition for optimal nutrient absorption in *A. paniculata*.

Influence of Mycorrhiza and Biofertilizers on Nutrient Uptake

Mycorrhizal and biofertilizer inoculations significantly enhance nutrient uptake efficiency. Aparna and Bagyaraj (2007) [3] demonstrated that *Glomus mosseae* and *Trichoderma harzianum* improved phosphorus uptake, biomass, and andrographolide concentration while reducing P fertilizer use by 25%. This improvement is attributed to increased root surface area, hyphal absorption, and phosphate solubilization. Mycorrhizae also enhance micronutrient uptake (Zn, Fe, Cu) and improve nutrient mobility through organic acid secretion. *Trichoderma* further enhances root exudation and chelation, demonstrating that microbial integration with INM strengthens nutrient acquisition and assimilation.

Effect of Integrated Nutrient Management on Macro- and Micronutrient Uptake

INM has been shown to improve both macro- and micronutrient uptake in Kalmegh compared with inorganic fertilization alone. Sanjutha *et al*. (2008) [27] found that FYM (15 t ha^{-1}) + NPK (75:75:50 kg ha^{-1}) + Panchagavya (3%) foliar spray yielded maximum N, P, and K uptake due to improved root proliferation and enzyme activity. Similarly, Tiwari *et al*. (2012) [32] reported higher nutrient uptake with FYM, vermicompost, and poultry manure than with inorganic sources, owing to gradual nutrient release and enhanced microbial turnover. Chaudhari *et al*. (2013) [5] confirmed that FYM at 7.5 t ha^{-1} significantly increased NPK content, reflecting better root absorption and improved soil physical properties.

Biochemical and Microbial Mechanisms Governing Nutrient Availability

Integration of organic and inorganic sources enhances microbial proliferation and enzymatic activity, promoting nutrient mineralization and cycling. Organic manures stimulate nitrogen fixers and phosphate solubilizers, increasing urease, phosphatase, and dehydrogenase activity. Verma *et al*. (2015) [35] observed that combining bio-inoculants (*Bacillus* sp., *Azospirillum*, *Phosphobacteria*) with fertilizers improved soil organic carbon, enzyme activity, and nutrient pools. Enhanced microbial respiration also releases CO_2 and carbonic acid, dissolving bound phosphates and micronutrients, thereby improving ion exchange and nutrient flux in the rhizosphere.

Role of Organic Matter in Micronutrient Mobilization

Organic amendments enhance micronutrient availability through chelation and complexation. Humic and fulvic acids in FYM and vermicompost form stable complexes with Fe, Zn, Mn, and Cu, improving their solubility and uptake. Vijaya *et al*. (2008) [36] demonstrated that coir-pith-based vermicompost improved soil nutrient status and Kalmegh growth even in alkaline conditions. Additionally, microbial siderophores enhance Fe and Mn solubility, while humic substances increase root permeability mechanisms vital for sustaining chlorophyll synthesis, enzymatic activity, and andrographolide biosynthesis.

Integration of Nitrogen Dynamics with Microbial Function

Organic sources and biofertilizers enhance nitrogen availability through gradual mineralization and biological fixation by *Azotobacter* and *Azospirillum*. The released ammonium and nitrate are efficiently assimilated via the GS-GOGAT pathway. Organic amendments minimize nitrogen losses through leaching and volatilization by improving soil structure and microbial immobilization. Integration with mineral fertilizers improves N-use efficiency, chlorophyll content, and protein synthesis, thereby increasing biomass and andrographolide yield (Hemalatha and Suresh, 2012; Tiwari *et al*., 2012) [12, 32].

Soil Fertility Improvement and Nutrient Retention

INM enhances soil fertility indices, nutrient retention, and long-term productivity. Organic matter increases CEC, aggregation, porosity, and water-holding capacity, promoting better root aeration and microbial colonization. Continuous INM application stabilizes soil pH, increases organic carbon, and maintains macro- and micronutrient availability, thereby improving soil health. Long-term studies confirm that INM not only boosts crop productivity but also restores soil fertility, supporting sustainable production systems for medicinal plants like Kalmegh.

2.1.4 Effect of Integrated Nutrient Management on Quality Parameters

Quality Attributes in Kalmegh: Physiological and Biochemical Basis

The phytochemical quality of *Andrographis paniculata* depends primarily on andrographolide, neoandrographolide, and deoxyandrographolide diterpenoid lactones synthesized via the methylerythritol phosphate (MEP) pathway in leaves and aerial tissues. Nutrient availability regulates secondary metabolite biosynthesis by influencing enzymatic activity, carbon-nitrogen balance, and energy metabolism. Adequate nitrogen supports chlorophyll formation and photosynthesis, providing carbon skeletons for metabolite synthesis, while phosphorus and potassium facilitate ATP generation, enzyme activation, and metabolite transport (Chiramel *et al*., 2006; Tiwari *et al*., 2012) [32]. Integrated Nutrient Management (INM) enhances these physiological processes by combining nutrient efficiency with improved soil health, leading to higher biomass and superior phytochemical quality.

Influence of Nitrogen Sources on Andrographolide Biosynthesis

Nitrogen plays a key role in regulating andrographolide content through its effect on the C:N ratio and metabolic allocation. Chauhan and Tiwari (2003) [32] reported that 40 kg N ha^{-1} applied through castor cake yielded the highest andrographolide (67.40 kg ha^{-1}) compared to control (31.50 kg ha^{-1}), owing to enhanced amino acid synthesis and chlorophyll content. Similarly, Tiwari *et al*. (2012) [32] observed that 60 kg N ha^{-1} from FYM produced the maximum andrographolide content (2.55%) and yield (93.16 kg ha^{-1}). The steady nutrient release from organic nitrogen sources sustains photosynthesis and metabolite biosynthesis, confirming the superior efficiency of organics in secondary metabolite regulation.

Effect of Phosphorus and Mycorrhizal Symbiosis

Phosphorus influences energy-dependent reactions crucial for diterpenoid biosynthesis. Aparna and Bagyaraj (2007) [3] demonstrated that inoculation with *Glomus mosseae* and *Trichoderma harzianum* enhanced phosphorus uptake, biomass, and andrographolide concentration, reducing phosphatic fertilizer use by 25%. This improvement is linked to greater P translocation and activation of 1-deoxy-D-xylulose 5-phosphate synthase (DXS) in the MEP pathway. Likewise, Chiramel *et al*. (2006) found that *Glomus leptotichum* inoculation significantly increased andrographolide content compared with *G. intraradices*. Mycorrhizal symbiosis thus enhances P-use efficiency and secondary metabolism, highlighting its value in quality-oriented INM practices.

Role of Organic Manures and Biofertilizers

Organic manures improve quality not only by nutrient supply but also through humic substances, phenolics, and biostimulants that influence metabolism. Sanjutha *et al*. (2008) [27] reported that FYM (15 t ha^{-1}) + NPK (75:75:50 kg ha^{-1}) + Panchagavya (3%) foliar spray significantly increased andrographolide content in Kalmegh, attributed to enhanced hormonal regulation and enzymatic activity. Hemalatha and Suresh (2012) [12] observed the highest andrographolide concentration (0.739%) under FYM (15 t ha^{-1}) + NPK (45:25:25 kg ha^{-1}) + *Azospirillum* (1 kg ha^{-1}), correlating with improved chlorophyll content and carbon fixation. Biofertilizers such as *Azospirillum*, *Azotobacter*, and *Phosphobacteria* further enhance N fixation, P solubilization, and phytohormone production, stimulating secondary metabolite biosynthesis.

Combined Role of Microbial Inoculants and Nutrient Integration

Microbial inoculants strengthen root-microbe interactions and enzyme-mediated nutrient mobilization, thereby promoting secondary metabolism. Ramesh *et al*. (2011) [25] reported that integrating vesicular arbuscular mycorrhiza (VAM) with inorganic fertilizers enhanced andrographolide concentration by improving nutrient uptake and maintaining an optimal C:N ratio. Khan *et al*. (2015) also found that vermicompost combined with *Azotobacter chroococcum* produced the highest andrographolide yield due to improved nitrogen assimilation and microbial enzyme activity. These microbial interactions and signaling compounds upregulate key genes in the diterpenoid biosynthetic pathway, reinforcing the synergistic role of biofertilizer-nutrient integration in improving both yield and phytochemical quality.

Improvement of Quality under Sustainable Systems

Verma *et al*. (2015) [35] reported that integrating bio-inoculants such as Bacillus sp. with NPK fertilizers increased andrographolide content by 61.3% in dried *Andrographis paniculata* leaves. This combined effect enhanced soil enzyme activity, organic carbon, and nutrient availability, thereby improving biosynthetic efficiency. Overall, integrated nutrient management promotes balanced carbon assimilation, nutrient partitioning, and secondary metabolism, achieving the dual goal of higher yield and superior phytochemical quality essential for medicinal plant production.

3. Physiological and Biochemical Mechanisms Underlying the Response of Kalmegh to Integrated Nutrient Management

3.1 Integrated Nutrient Management as a Regulator of Plant Metabolism

The physiological performance of *Andrographis paniculata* is governed by nutrient balance, photosynthetic efficiency, and metabolic regulation. Integrated Nutrient Management (INM) influences growth and phytochemical accumulation by enhancing nutrient assimilation, enzyme activity, and hormonal equilibrium. The combined use of organic, inorganic, and biological nutrient sources ensures a steady and synchronized nutrient supply throughout the crop cycle, supporting both primary and secondary metabolism. Organic manures such as FYM and vermicompost provide slow nutrient release through microbial mineralization, while inorganic fertilizers meet immediate crop demands. This nutrient synchronization minimizes stress, stabilizes chlorophyll, and sustains carbon assimilation the foundation for growth and andrographolide biosynthesis (Hemalatha and Suresh, 2012; Tiwari *et al*., 2012) [12, 32].

3.2 Enhancement of Photosynthetic Efficiency and Carbon Assimilation

INM enhances photosynthetic efficiency in Kalmegh by improving nitrogen, phosphorus, and potassium nutrition. Nitrogen, a key component of chlorophyll and Rubisco, increases chlorophyll density, leaf area index (LAI), and carbon fixation rate. Phosphorus supports ATP synthesis for energy transfer, while potassium regulates stomatal conductance, enzyme activation, and carbohydrate translocation, strengthening the source-sink relationship essential for metabolite synthesis (Chauhan and Tiwari, 2003) [6]. Organic and biofertilizer inputs further protect chloroplasts through micronutrient cofactors (Zn, Fe, Mn), which enhance antioxidant enzyme activity and maintain photosynthetic integrity under stress.

3.3 Root System Modulation and Nutrient Uptake Dynamics

INM improves root morphology, root hair density, and rhizospheric aeration while promoting beneficial microbial symbioses. Inoculation with *Glomus mosseae* and *Trichoderma harzianum* enhances phosphorus uptake, biomass, and fertilizer-use efficiency (Aparna and Bagyaraj, 2007) [3]. Mycorrhizal hyphae and microbial secretions (organic acids, phosphatases) solubilize bound nutrients, alter rhizospheric pH, and increase ion availability. These interactions strengthen nutrient acquisition and stimulate root exudation, creating a feedback loop that enhances mineralization and plant vigour.

3.4 Enzymatic Regulation of Nitrogen and Carbon Metabolism

Balanced nutrient availability under INM elevates the activity of key enzymes in nitrogen and carbon metabolism. Nitrate reductase (NR) and glutamine synthetase (GS) promote nitrogen assimilation into amino acids via the GS-GOGAT pathway, while phosphorus and potassium regulate sucrose synthase and ATPase activities involved in energy transfer and assimilate transport. Maintaining optimal C:N homeostasis ensures efficient carbon allocation toward both structural growth and secondary metabolite synthesis, explaining the higher herbage yield and andrographolide content under integrated treatments (Hemalatha and Suresh, 2012; Ramesh *et al*., 2011) [12, 25].

3.5 Hormonal Modulation and Growth Regulation

INM influences endogenous hormone balance by stimulating both plant and microbial hormone production. *Azospirillum* and *Azotobacter* release auxins and gibberellins that enhance root elongation, branching, and leaf initiation, while humic-rich manures promote cytokinin-like activity supporting cell division and leaf longevity. Balanced hormonal regulation improves assimilate partitioning and photosynthate transport, maintaining physiological activity under variable conditions. This hormonal synergy contributes to greater branching, leaf expansion, and prolonged vegetative growth in Kalmegh (Sharma, 2016) [30].

3.6 Role of Biofertilizers and Microbial Interactions

Biofertilizers form a biological link between soil nutrients and plant metabolism. *Azotobacter* and *Azospirillum* fix atmospheric nitrogen, *Phosphobacteria* solubilize phosphate, and *Trichoderma harzianum* enhances nutrient cycling and stress tolerance. Their interactions with organic and inorganic inputs increase enzymatic activity (urease, phosphatase, and dehydrogenase) and microbial biomass carbon. Microbial volatile compounds (VOCs) and metabolites act as signaling molecules, upregulating genes like *GGPPS* and *AndroSyn* in the diterpenoid biosynthetic pathway. This demonstrates that INM enhances andrographolide production through both nutritional and biochemical regulation (Verma *et al*., 2015; Khan *et al*., 2015) [35].

3.7 Antioxidant and Stress-Response Mechanisms

INM mitigates oxidative stress by enhancing the activity of antioxidant enzymes such as SOD, CAT, and POD. Micronutrients (Fe, Mn, Cu, Zn) supplied through organics and biofertilizers act as cofactors for these enzymes, maintaining redox balance and protecting chloroplast membranes. Improved nutrient balance sustains photosynthetic function and activates defense-related secondary metabolism, linking oxidative stress reduction with increased andrographolide biosynthesis.

3.8 Secondary Metabolism and Andrographolide Biosynthesis

Andrographolide synthesis in Kalmegh occurs via the methylerythritol phosphate (MEP) pathway in plastids, regulated by enzymes such as DXR and GGPPS. Adequate availability of N, P, and Mg enhances these enzymatic reactions by providing energy (ATP, NADPH) and cofactors. Potassium and micronutrients stabilize enzyme activity and maintain redox balance during metabolite formation. Thus, INM supports both substrate supply and enzyme activation, resulting in higher andrographolide accumulation (Chauhan and Tiwari, 2003; Hemalatha and Suresh, 2012; Verma *et al*., 2015) [6, 12, 35].

3.9 Soil-Plant-Microbe Interactions and Rhizospheric Ecology

INM fosters a dynamic rhizospheric ecosystem characterized by enhanced microbial diversity and nutrient cycling. Organic substrates stimulate microbial respiration and organic acid secretion, improving nutrient solubilization and soil aggregation. Beneficial microbes and root exudates form a positive feedback loop that strengthens nutrient turnover and biological fertility. This enriched rhizospheric ecology under INM enhances soil enzyme activity, nutrient flux, and long-term productivity, establishing a stable foundation for sustainable Kalmegh cultivation and phytochemical quality assurance.

4. Challenges, Research Gaps, and Future Prospects

4.1 Present Limitations in Nutrient Management for Medicinal Crops

Despite advances in integrated nutrient management (INM) for food crops, its application in medicinal plants like *Andrographis paniculata* remains constrained by scientific and practical limitations. Medicinal plants are typically grown under marginal conditions with low fertility and limited input use (Verma *et al*., 2015) [35]. The absence of crop-specific nutrient recommendations often leads to unbalanced or suboptimal fertilizer applications, which can restrict yield or reduce andrographolide content. Variability in soil type, organic matter, and climate also causes inconsistent responses to INM across regions. The lack of soil fertility mapping and decision-support tools further limits precision nutrient management in Kalmegh cultivation.

4.2 Quality Standardization and Secondary Metabolite Variability

A major research gap lies in linking nutrient regimes with phytochemical standardization. Although INM improves andrographolide yield and concentration, the underlying nutrient-gene-metabolite relationships remain poorly understood. Variations in organic matter quality, microbial diversity, and micronutrient availability contribute to inconsistency in andrographolide content, complicating pharmaceutical standardization. Excessive mineral fertilization may also suppress secondary metabolism or lead to nitrate accumulation, compromising raw material quality (Tiwari *et al*., 2012; Khan *et al*., 2015) [32]. Future studies integrating nutrient physiology, metabolomics, and transcriptomics are essential to develop precision nutrient strategies that ensure uniform yield and bioactive compound content.

4.3 Soil Health and Microbial Decline under Intensive Cultivation

Continuous or unbalanced fertilization deteriorates soil health by reducing microbial diversity and enzyme activity. Poor-quality organic manures can introduce heavy metals or phytotoxins, negatively affecting nutrient cycling and secondary metabolite production (Sanjutha *et al*., 2008) [27]. Additionally, the field performance of microbial inoculants like *Azospirillum*, *Phosphobacteria*, and *Trichoderma* often declines under heat, moisture stress, or chemical interference. Improving inoculant stability, compatibility, and formulation technology is crucial for consistent microbial efficiency and long-term soil fertility.

4.4 Integration of Micronutrients, Nanofertilizers, and Biostimulants

Micronutrient management in Kalmegh remains underexplored despite its vital roles in enzyme activation, chloroplast function, and redox regulation. Nanofertilizers offer promising prospects for improving nutrient-use efficiency and minimizing losses through controlled nutrient release and better root uptake (Ranjan *et al*., 2023). However, their optimal dosage and ecological impact require careful evaluation. Biostimulants such as seaweed extracts, humic acids, and microbial metabolites can further enhance nutrient uptake, photosynthesis, and stress resilience by acting as metabolic activators supporting higher andrographolide synthesis and plant vigour.

4.5 Need for Precision and Digital Nutrient Management
Conventional fertilization practices ignore spatial and temporal variability in nutrient dynamics. Precision nutrient management, enabled by remote sensing, soil sensors, and AI-based decision systems, can revolutionize INM in medicinal crops. Tools such as NDVI, chlorophyll fluorescence imaging, and soil conductivity mapping allow real-time monitoring of plant nutrition. Integrating these with IoT-based nutrient delivery can ensure site-specific and demand-driven fertilization. Developing crop-specific digital models linking spectral reflectance, nutrient status, and andrographolide accumulation remains an emerging frontier requiring multidisciplinary collaboration.

4.6 Ecological and Environmental Considerations
Although INM reduces reliance on synthetic fertilizers, its ecological footprint must be quantified. Poorly managed organic inputs may emit greenhouse gases or create anaerobic soil conditions, affecting root respiration. Incorporating biochar into INM systems can enhance nutrient retention, microbial activity, and carbon sequestration. Evaluating life-cycle emissions, nutrient recovery efficiency, and energy balance will align Kalmegh cultivation with climate-smart and regenerative agriculture goals, ensuring environmental sustainability alongside productivity.

4.7 Research Gaps and Priority Areas
Despite extensive evidence supporting INM efficacy, several critical research gaps persist. A deeper mechanistic understanding is required on how nutrient combinations regulate gene expression and enzyme kinetics in andrographolide biosynthesis. The integration of micronutrients, nanofertilizers, and biostimulants within INM frameworks remains underexplored. Quantification of nutrient-use efficiency indices (NUE, PUE, KUE) and their linkage to yield and secondary metabolite production is limited. Standardized, climate-resilient biofertilizer formulations are needed for consistent field performance. Long-term studies on soil fertility and microbial dynamics under continuous INM adoption are scarce. Additionally, digital decision-support tools for precision INM and socioeconomic analyses to assess farmer adoption barriers and cost-benefit ratios are essential. Addressing these gaps will refine INM strategies for Kalmegh and establish a scalable model for sustainable nutrient management in medicinal and aromatic crops.

4.8 Future Prospects and Strategic Directions
The future of nutrient management in *Andrographis paniculata* lies in merging traditional organic practices with modern biotechnological and digital advancements. Key strategic directions include:

- **Integrated Biofertilizer Consortia:** Development of multi-strain microbial formulations combining nitrogen-fixing, phosphate-solubilizing, and hormone-producing microbes for synergistic nutrient mobilization.
- **Nanotechnology in INM:** Use of nano-chelated micronutrients, nano-zeolite carriers, and slow-release nanofertilizers to improve nutrient efficiency and reduce environmental losses.
- **Systems Biology Approaches:** Application of transcriptomics, proteomics, and metabolomics to identify nutrient-responsive genes governing andrographolide biosynthesis.
- **Climate-Resilient INM Protocols:** Designing nutrient regimes that enhance physiological resilience under abiotic stresses such as heat, drought, and salinity.
- **Agro-Ecological Intensification:** Integration of INM with intercropping, mulching, and organic residue recycling for regenerative production systems.
- **Digital Nutrient Advisory Systems:** Deployment of AI-based and smartphone-enabled tools for real-time, site-specific nutrient recommendations.

Conclusion
Integrated Nutrient Management (INM) in *Andrographis paniculata* effectively enhances growth, yield, and andrographolide accumulation through the balanced integration of organic, inorganic, and biological nutrient sources. Treatments such as 15 t FYM ha^{-1} + 75:75:50 kg NPK ha^{-1} + Panchagavya (3%) or 10-15 t vermicompost ha^{-1} + 50% RDF + biofertilizers have achieved dry herbage yields up to 2.6 t ha^{-1} and andrographolide content up to 2.5%. INM improves photosynthetic efficiency, enzymatic regulation, and nutrient-use efficiency while enriching soil organic carbon and microbial activity. With benefit-cost ratios ranging from 2.0 to 7.0, INM ensures sustainable, high-quality, and eco-efficient Kalmegh production under diverse agro-ecological conditions.

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