

L-Lysine: A Comprehensive Review of Biosynthesis Pathways, Industrial Production Methods and Diverse Uses

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Abstract

Background and Objective: L-Lysine, an essential amino acid, plays critical roles in protein synthesis, metabolic regulation and structural integrity. This review aimed to comprehensively summarize the amino acid chemical characteristics, biosynthesis pathways, industrial production strategies and diverse uses in nutrition, medicine and biotechnology.

Literature Search Strategy: A literature search was carried out using PubMed, Scopus and Web of Science up to 2025. Keywords included "L-lysine", "biosynthesis", "fermentation", "*Corynebacterium glutamicum*" and "applications". Relevant original research, reviews and patents from major patent authorities (e.g., USPTO, WIPO and EPO) were critically assessed. As a narrative review, the synthesis focused on providing a broad overview of the field rather than a quantitative meta-analysis.

Results and conclusion: The diaminopimelic acid pathway in bacteria and plants and the α -aminoadipic acid pathway in fungi were detailed. Industrial production depended on engineered *Corynebacterium glutamicum* strains with feedback-resistant aspartokinase, optimized biotin levels and downstream ion-exchange purification. Key uses included animal feed supplementation, antiviral therapy, bone health, anxiety reduction and emerging roles in cancer immunotherapy. Recent advances in CRISPR/Cas9, metabolic flux analysis and sustainable feedstocks were highlighted. L-Lysine is a cornerstone of the global bioeconomy with expanding pharmaceutical and material uses. Precision metabolic engineering and circular bioeconomy approaches drive further innovations.

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What is "already known" on this topic:

- L-lysine is an essential amino acid with well-established roles in protein synthesis, collagen cross-linking, and calcium homeostasis.
- Industrial production relies on fermentation using *Corynebacterium glutamicum* with feedback-resistant aspartokinase and optimized biotin levels.
- Supplementation of lysine in animal feed improves growth performance and reduces nitrogen excretion; its antiviral activity against herpes simplex virus has been clinically documented.

What this article adds:

- Provides an integrated overview of L-lysine from fundamental biosynthesis (DAP and AAA pathways) to industrial-scale production and emerging pharmaceutical applications within a single framework.
- Highlights recent advances in CRISPR/Cas9 genome editing, metabolic flux analysis, and AI-driven bioprocess optimization for sustainable lysine production.
- Discusses novel roles of lysine metabolism in cancer immunotherapy via histone crotonylation and its potential in neuropharmacology as a serotonin receptor modulator, which are not covered in previous reviews.

1. INTRODUCTION

L-Lysine [(2S)-2,6-diaminohexanoic acid] is an essential α -amino acid of critical biological importance [1]. Structurally, L-lysine is distinguished by its unique four-carbon aliphatic side chain terminating in a primary ϵ -amino group [2]. This ϵ -amino moiety, with a dissociation constant (pK_{a3}) of approximately 10.53, renders the molecule fundamentally basic and positively charged at physiological pH [2]. Such electrochemical characteristics are not merely incidental as they allow L-lysine to participate in critical electrostatic interactions within the tertiary and quaternary structures of proteins, facilitating the formation of salt bridges that stabilize protein folding [3]. Furthermore, the presence of two amino groups—one at the α -position and one at the ϵ -position - grants L-lysine a versatile reactivity profile, making it a central substrate for diverse post-translational modifications, including acetylation, methylation, ubiquitination and hydroxylation. For nutrition, L-lysine is classified as a strictly essential (indispensable) amino acid for humans and monogastric animals [1]. Unlike nonessential amino acids (NEAA), the mammalian metabolic repertoire lacks the enzymatic machinery, specifically the enzymes of the diaminopimelic acid (DAP) or α -aminoadipic acid (AAA) pathway, to synthesize the lysine carbon skeleton *de novo*. Therefore, the bioavailability of L-lysine is a limiting factor in cellular growth, tissue repair and overall metabolic homeostasis.

The biological significance of L-lysine extends into a multifaceted array of physiological systems, most significantly within the synthesis and maturation of the extracellular matrix. L-Lysine is an indispensable precursor for the biosynthesis of collagen, the primary structural protein in mammals. Within the endoplasmic reticulum, specific lysine residues on procollagen chains are hydroxylated by the enzyme of lysyl hydroxylase to form hydroxylysine [4]. These residues are then glycosylated and, upon secretion into the extracellular space, are oxidatively deaminated by lysyl oxidase to form highly reactive aldehydes. These aldehydes facilitate the covalent cross-linking between collagen fibrils, providing the tensile strength and structural integrity needed for skin, tendons, cartilage and the bone matrix [1]. In addition to structural roles, L-lysine is the fundamental precursor for the endogenous synthesis of L-carnitine. This process, which begins with the trimethylation of lysine residues within specific proteins, eventually yields free carnitine, which is

essential for the transport of long-chain fatty acids (LCFA) within the inner mitochondrial membrane for β -oxidation [5]. This link establishes L-lysine as an underappreciated critical regulator of lipid metabolism and systemic energy production.

Clinically, the therapeutic potential of L-lysine is underpinned by its unique interaction with other cationic amino acids and minerals. A primary area of interest involves its role in calcium homeostasis. Research suggests that L-lysine enhances the intestinal absorption of Ca^{2+} ions and concomitantly improves the renal conservation of calcium, thereby playing a potential role in the prevention and adjunct treatment of osteoporosis [6]. Furthermore, L-lysine demonstrates a well-documented antagonistic relationship with L-arginine. Many neurotropic viruses, particularly the herpes simplex virus (HSV), rely heavily on arginine-rich proteins for viral replication and capsid assembly. By acting as a competitive inhibitor for arginine transport and metabolism, high concentrations of L-lysine can effectively suppress viral shedding and accelerate the healing of herpetic lesions [7]. Emerging evidence also points toward a neuro-modulatory role, where L-lysine may act as a partial antagonist to serotonin (5-HT₄) receptors, potentially mitigating stress-induced anxiety and modulating cortisol responses in human populations [8].

The transition of L-lysine from a laboratory curiosity to a cornerstone of the global bioeconomy is a testament to the advancements in metabolic engineering and industrial fermentation [9]. Currently, the global demand for L-lysine exceeds 2.5 million metric tons annually, with a market valuation that increases significantly as the global population increases [1]. The animal feed industry is the primary consumer, where L-lysine is used as a critical additive to balance the nutritional profile of cereal-based diets. In conventional corn-soybean based diets for porcine and poultry, L-lysine is typically the first limiting amino acid. Its deficiency prevents the optimal use of all other dietary amino acids, leading to poor feed conversion ratios and increased nitrogen excretion, which poses environmental challenges. It is noteworthy that the identity of the first limiting amino acid varies with the cereal base of the diet. For example, threonine may become limited in wheat-based rations, while methionine or lysine can be co-limited in rice-based diets. By supplementing animal diets with crystalline L-lysine, producers can decrease the total



crude protein content of the feed, often by replacing expensive soybean meal with cheaper corn, while maintaining superior muscle deposition and growth rate [10].

For humans, the industrial use of L-lysine is diverse. It is widely used in the pharmaceutical industry for the formulation of intravenous nutritional solutions, dietary supplements and as a counter-ion to improve the solubility of acidic drugs such as ibuprofen (lysine ibuprofenate) [11]. The food industry uses L-lysine for the fortification of grain products such as bread and flour, particularly in regions where protein-energy malnutrition is endemic and the diet is predominantly cereal based [12]. Historically, L-lysine was produced via complex chemical synthesis or through the hydrolysis of protein-rich wastes; however, these methods were affected by low yields and the production of racemic mixtures (DL-lysine). The modern era is defined by green biotechnology, where the fermentation of renewable feedstocks such as glucose, sucrose and molasses allows for the sustainable, enantio-pure production of L-lysine at an industrial scale using hyper-producing strains of *Corynebacterium glutamicum* [9]. Based on the increasing research in metabolic flux analysis, genomic editing and the expanding clinical use of amino acids, there is a profound necessity for a synthesized, high-level overview of L-lysine. While several recent reviews have addressed specific aspects such as lysine metabolism in humans, physiological roles and crop biofortification, a critical gap is in integrating the complete value chain from fundamental biosynthesis to industrial-scale production and diverse uses within a single framework.

Importantly, the landscape has evolved rapidly since the most recent comprehensive reviews. In metabolic engineering, CRISPR/Cas9 has enabled precise knockout of competing pathways and promoter engineering for key biosynthetic genes, for example, replacement of the *aceE* promoter with the *dapA*-A16 promoter has improved L-lysine production by up to 100% in *C. glutamicum* while overexpression of the *lysE* exporter has been shown to improve feedback inhibition and enhance amino acid efflux. Moreover, lysine catabolism has emerged critically in tumor immunology, with recent studies demonstrating that reprogramming of lysine metabolism in glioblastoma stem cells increases histone crotonylation and promotes immune evasion. In sustainable production, engineered *C. glutamicum* strains enable co-use of glucose and xylose from lignocellulosic feedstocks, overcoming carbon catabolite

repression, while AI-driven digital twins and soft-sensing technologies are transforming real-time bioprocess control. By connecting these traditionally siloed domains, this review has provided a holistic perspective that is absent from the current literature. Ultimately, this review has integrated classical biochemistry with emerging frontiers, particularly lysine role in cancer immunotherapy and sustainable biorefining, to provide a holistic framework for researchers and industries.

2. METHOD: LITERATURE SEARCH STRATEGY

To ensure comprehensive and transparent coverage, a structured literature search was carried out in PubMed, Scopus and Web of Science for articles published up to 2025. The search strategy combined the following keywords of "L-lysine", "biosynthesis", "diaminopimelic acid pathway", " α -aminoadipic acid pathway", "fermentation", "*Corynebacterium glutamicum*", "industrial production" and "applications". Only peer-reviewed original research articles, authoritative review papers and relevant patents from major patent authorities (e.g., USPTO, WIPO, EPO) were considered. Duplicate records were removed and the references were screened based on their relevance to the scope of this review. The findings were synthesized narratively, with an emphasis on key mechanistic insights, industrial advancements and emerging therapeutics.

3. CHEMICAL AND PHYSICAL CHARACTERISTICS OF L-LYSINE

3.1. Molecular Architecture and Stereochemical Isomerism

L-Lysine, systematically designated as (S)-2,6-diaminohexanoic acid (where 'L' corresponds to the (S)-configuration at the chiral α -carbon), is characterized by a six-carbon aliphatic backbone. Its molecular formula, $C_6H_{14}N_2O_2$, corresponds to a molecular weight of approximately $146.19 \text{ g mol}^{-1}$. The structural hallmark of this molecule is the presence of two primary amino groups of the α -amino group attached to the chiral C2 atom and the terminal ϵ -amino group located at the distal end of the side chain. This diamino configuration, coupled with a single carboxyl group, classifies lysine as a basic amino acid. In an aqueous environment at physiological pH (nearly 7.4), the two amino groups are typically protonated ($-NH_3^+$), while the carboxyl group is deprotonated ($-COO^-$), providing the



molecule net positive charge and high isoelectric point (pI) of 9.74 [13]. The presence of the asymmetric α -carbon atom creates two distinct enantiomers of L-lysine and D-lysine. In biological systems, the L-isomer is the exclusive form used for ribosomal protein synthesis. The D-isomer, while chemically similar, is not recognized by mammalian ribosomes for protein synthesis and has negligible nutritional value, as the enzymatic conversion of D-lysine to the L-form is inefficient in mammals [14]. This stereospecificity is a critical factor in industrial production. While chemical synthesis often results in a racemic mixture (DL-lysine), biotechnological fermentation using *C. glutamicum* is highly advantageous because it is inherently stereoselective, yielding 100% optically pure L-lysine [15]. The commercial preference for the L-form is absolute, as the D-form lacks nutritional value for livestock and humans.

3.2. Solubility, Hydration and Ionization States

The physical behavior of L-lysine is greatly affected by its ionization state, which is a function of the surrounding pH. The molecule possesses three distinct dissociation constants (pK_a) of pK_{a1} (carboxyl) $\approx$ 2.18, pK_{a2} (α -amino) $\approx$ 8.95 and pK_{a3} (ϵ -amino) $\approx$ 10.53. This tri-protic nature allows lysine to act as an effective buffer in specific pH ranges. For solubility, L-lysine is highly hydrophilic. It demonstrates exceptional solubility in water, reaching concentrations of approximately 64.2 g per 100 ml at 25 °C. This high solubility is due to the extensive hydrogen-bonding capabilities of its two amino groups and the carboxylate group with water molecules. In contrast, it is practically insoluble in non-polar organic solvents such as diethyl ether and benzene and slightly soluble in ethanol. In industries, the high-water solubility is a benefit and a challenge; while it facilitates easy incorporation into liquid supplements and uniform distribution in fermentation broths, it necessitates energy-intensive evaporation and crystallization steps during downstream processing to recover the solid product.

3.3. Industrial Stability and the Monohydrochloride Salt Form

In its free base form, L-lysine is quite hygroscopic (readily absorbing moisture from the atmosphere) and can be chemically unstable over long times. To overcome these limitations, the global industry predominantly produces and trades L-lysine in its salt form, specifically L-lysine monohydrochloride (L-lysine HCl). This form is characterized by significantly improved stability, higher

melting point (approximately 263 °C) and less hygroscopic nature, compared to the free base [16].

The stability of L-lysine during industrial processing, particularly during the pelleting or extrusion phases of animal feed manufacturing, is a major concern for nutritionists. While L-lysine HCl is thermally stable under moderate heat, it is highly susceptible to the Maillard reaction. Because of the highly reactive and nucleophilic nature of the ϵ -amino group, L-lysine can react with reducing sugars (such as glucose and lactose) in the feed matrix when exposed to heat and moisture. This reaction forms Maillard products (fructose-lysine and melanoidins), which render the lysine biologically unavailable to the animals. Therefore, industrial processing must carefully be calibrated to minimize heat damages, ensuring that the added L-lysine is nutritionally reactive and absorbable in the small intestine.

3.4. Spectroscopic and Analytical indicators

For quality assurance in industrial and clinical settings, the physical characteristics of L-lysine are monitored through specific analytical techniques. Its optical rotation is a primary marker for purity, with a specific rotation $[\alpha]_D^{25}$ typically ranging between +25.5° and +26.0° (5 N HCl). Furthermore, the ϵ -amino group allows for specific colorimetric detection using reagents such as ninhydrin, which produces a characteristic purple color or 2,4,6-trinitrobenzene sulfonic acid (TNBS). Modern high-performance liquid chromatography (HPLC) with cation-exchange columns is the gold standard for quantifying lysine levels in complex matrices, depending on the molecule unique charge-to-mass ratio and its predictable elution profile at specific pH gradients. Table 1 summarizes key physicochemical characteristics of lysine, including molecular weight, isoelectric point, solubility and dissociation constants).

4. BIOSYNTHESIS PATHWAYS (CORE MECHANISM)

The elucidation of L-lysine biosynthesis represents one of the most significant chapters in microbial biochemistry, revealing an extraordinary evolutionary divergence. Unlike several other amino acids that share a universal biosynthetic route within all domains of life, L-lysine is synthesized via two entirely distinct and non-homologous pathways of DAP pathway in bacteria and plants and AAA pathway, exclusive to fungi and certain algae [17].



Table 1. Physicochemical characteristics of L-lysine

Property	Value/Description
Chemical Name	(2S)-2,6-diaminohexanoic acid
Molecular Formula	C ₆ H ₁₄ N ₂ O ₂
Molecular Weight	~146.19 g/mol
Isoelectric Point (pI)	9.74
Water Solubility	64.2 g/100 mL at 25°C
Dissociation Constants	pK _a 1 (carboxyl) ≈ 2.18 pK _a 2 (α-amino) ≈ 8.95 pK _a 3 (ε-amino) ≈ 10.53
Optical Rotation	[α] _D ²⁵ between +25.5° and +26.0° (in 5N HCl)

Table 2 summarizes the key differences between the DAP and AAA pathways, including the respective organisms, carbon sources and key intermediates. This metabolic dichotomy is a cornerstone of evolutionary biology and forms the basis for the massive industrial scales of production.

4.1. The Diaminopimelic Acid Pathway: the Bacterial and Botanical Route

The DAP pathway is a sophisticated branch of the aspartate family of amino acids, which encompasses the synthesis of methionine, threonine and isoleucine. In the industrial *C. glutamicum* and higher plants, this begins with the phosphorylation of L-aspartate to L-aspartyl phosphate, a reaction catalyzed by the enzyme aspartokinase (AK; EC 2.7.2.4) [18]. This initial step is highly energetic, needing ATP as a phosphate donor. The resulting aspartyl phosphate decreases to aspartate-β-semialdehyde (ASA) by the enzyme of aspartate-semialdehyde dehydrogenase (ASD; EC 1.2.1.11). The pathway reaches its most critical branching point. While ASA can be diverted to synthesis of homoserine (then threonine and methionine), the commitment to L-lysine synthesis occurs through the condensation of ASA with pyruvate. This reaction,

mediated by dihydrodipicolinate synthase (DHDPS; EC 4.3.3.7), forms 4-hydroxy-tetrahydrodipicolinate, effectively sealing the fate of the carbon skeleton to lysine.

Then, a series of enzymatic transformations, including reduction, succinylation (or acetylation in some species), transamination and deacylation, leads to the formation of the symmetrical intermediate meso-2,6-diaminopimelate (meso-DAP). In bacteria, meso-DAP is not merely a precursor to lysine; it serves a dual role as an essential cross-linking agent in the peptidoglycan layer of the cell wall, highlighting the intrinsic link between amino acid metabolism and structural integrity. The final step in the pathway is the irreversible decarboxylation of meso-DAP, catalyzed by diaminopimelate decarboxylase (LysA; EC 4.1.1.20), which yields the final product of L-lysine [19]. In higher plants, this pathway is strictly localized within the chloroplasts, using photosynthetic energy and carbon intermediates to maintain the plant's nutritional requirements.

4.2. The α-aminoadipic Acid Pathway: the Fungal Strategy

In contrast to the aspartate-derived route, fungi (e.g., yeasts) and certain euglenoid algae use the AAA pathway, which originates from the tricarboxylic acid (TCA) cycle. The carbon skeleton is derived from the condensation of α-ketoglutarate and acetyl-CoA to form homocitrate. This reaction is catalyzed by homocitrate synthase (EC 2.3.3.14) and is analogous to the synthesis of citrate from oxaloacetate in the standard TCA cycle. Through a series of isomerizations and oxidations—resembling a shifted version of the early TCA cycle steps—homocitrate is converted to α-ketoadipate.

Table 2. Comparison of L-lysine biosynthesis pathways

Feature	DAP Pathway	AAA Pathway
Organisms	Bacteria and plants	Fungi and certain algae
Carbon Source	L-aspartate	α-ketoglutarate and acetyl-CoA
Key Intermediate	meso-2,6-diaminopimelate (meso-DAP)	Saccharopine
Final Step Enzyme	Diaminopimelate decarboxylase (LysA)	Saccharopine dehydrogenase
Biological Role	Essential for peptidoglycan cross-linking	Derived from the TCA cycle

The conversion of α-ketoadipate to L-lysine involves several unique enzymatic steps, including AAA, through



transamination [20]. The subsequent reduction of the δ -carboxyl group of AAA to an aldehyde (catalyzed by α -aminoacidopate reductase) is a complex, multi-domain enzymatic process, which proceeds via a two-step mechanism of ATP-dependent adenylation followed by NADPH-dependent reduction. The final amination step produces saccharopine, which is oxidatively cleaved by saccharopine dehydrogenase to yield L-lysine and α -ketoglutarate. The presence of the AAA pathway in fungi and its absence in bacteria and animals highlights a profound evolutionary split. Because humans lack the DAP and AAA pathways, L-lysine is rendered an essential dietary requirement, as the mammalian genome contains no homologs for these complex multiple-step enzymes.

4.3. Regulatory Architecture and Feedback Mechanisms

The regulation of L-lysine biosynthesis is an exquisite display of cellular economy, designed to prevent the over-accumulation of metabolites. However, for industrial bioprocessing, these regulatory brakes must strategically be bypassed. The primary regulatory node in the DAP pathway is aspartokinase (AK) [18]. In wild-types, AK is subject to concerted feedback inhibition; the enzyme is active if L-lysine or L-threonine is present in excess, but it is dramatically inhibited when the two amino acid accumulation simultaneously. This AND-gate [known as concerted (sequential) feedback inhibition] logic ensures that the cell does not halt production of the shared precursor ASA unless all downstream branches are saturated.

A secondary but equally vital regulatory point is dihydrodipicolinate synthase (DHDPS). As the first committed enzyme of the lysine branch, DHDPS is highly sensitive to feedback inhibition by L-lysine alone [21]. In a typical cellular environment, as L-lysine levels increase, the

molecule binds to the allosteric site of DHDPS, inducing a conformational change that decreases its affinity for ASA [21]. This prevents the wasteful flux of carbon, when the lysine pool is sufficient. Furthermore, gene-level regulation such as the *lysC* and *lysA* operon control, manages the total enzyme concentration within the cell.

In industrial strain development, scientists use auxotrophic mutants (e.g., strains that cannot produce threonine) to eliminate the concerted inhibition of AK [22]. Alternatively, they select for regulatory mutants, often resistant to the lysine analog S-(2-aminoethyl)-L-cysteine (AEC), typically due to mutations in aspartokinase that render its allosteric site insensitive to lysine though mutations in lysine transporters or other regulatory proteins can contribute to resistance. These engineered enzymes do not recognize L-lysine as an inhibitor, allowing the metabolic flux to continue unabated, which is the fundamental requirement for the hyper-production of L-lysine in large-scale bioreactors.

5. INDUSTRIAL PRODUCTION STRATEGIES

The industrial production of L-lysine represents a triumph of modern biotechnology, transitioning from rudimentary chemical synthesis to highly sophisticated, large-scale microbial fermentation. This evolution has been driven by the dual necessity of meeting the astronomical global demand for animal feed additives, while adhering to green chemistry principles that prioritize high enantiomeric purity, renewable feedstocks and cost-efficiency (Table 3). Currently, the global production landscape is dominated by the use of hyper-producing bacterial strains that have metabolically been rewired to bypass natural homeostatic constraints.

Table 3. Assessment of the L-lysine industrial production methods

Method	Advantages	Disadvantages/Limitations
Microbial fermentation	Highly stereoselective (100% L-form); uses renewable feedstocks; sustainable	Requires energy-intensive downstream processing for product recovery
Enzymatic biocatalysis	Absolute stereoselectivity; ultra-high purity; simplifies purification	High cost of precursors (e.g., caprolactam) limits it to pharmaceutical use
Chemical synthesis	Historical method using petrochemicals	Non-stereospecific (DL-Lysine mixture); produces nutritionally inert D-isomer



5.1. The Microbial Chassis: *Corynebacterium glutamicum*

The backbone of the global lysine industry is undoubtedly the Gram-positive, non-sporulating soil *C. glutamicum* and its close relatives. These organisms were first identified in the mid-20th century for their innate ability to secrete glutamic acid. Through decades of classical mutagenesis and modern genetic engineering, they have been transformed into cell factories for L-lysine. The microorganism is particularly favored due to its robust growth characteristics, lack of extracellular protease activity and a relatively simple metabolic network that is responsive to large-scale flux manipulation. In an industrial context, wild-type strains are outdated; instead, manufacturers use regulatory mutants that are insensitive to the concerted feedback inhibition of aspartokinase. These strains often carry specific mutations in the *lysC* gene, ensuring that the metabolism occurs even when intracellular lysine concentrations reach levels that normally trigger a total biosynthetic shutdown. Furthermore, the use of auxotrophic mutants such as homoserine or threonine-auxotrophs ensures that the carbon flux is not diverted to competing pathways, effectively funneling a majority of the aspartate-semialdehyde pool directly into DAP branch.

5.2. Bioprocess Engineering: Medium Optimization and the Biotin Regulatory Paradox

The productivity of a fermentation cycle is intrinsically linked to the optimization of the culture media and the environmental parameters within the bioreactor. The primary carbon sources used in industrial scales are typically inexpensive agricultural byproducts, most significantly cane or beet molasses, hydrolyzed cornstarch and sucrose. The feasibility of using molasses for amino acid production has been demonstrated in various studies, including the production of L-tryptophan from cane and beet molasses [23]. These substrates are metabolized through the glycolytic pathway and the pentose phosphate pathway (PPP) to provide the necessary precursors, pyruvate and oxaloacetate and the reducing power (NADPH) needed for lysine assembly. Nitrogen is typically supplied in the form of anhydrous ammonia or ammonium salts, which serves a dual purpose as a pH-regulating agent, maintaining the broth at a near-neutral level to prevent acid-induced metabolic inhibition.

A defining characteristic of L-lysine fermentation is the biotin effect. Biotin (vitamin B7) serves as an essential cofactor for pyruvate carboxylase, the enzyme responsible for the anaplerotic replenishment of oxaloacetate from pyruvate [24]. In the industrial production of amino acids, the concentration of biotin is accurately controlled to create a state of sub-optimal growth. This limitation decreases the activity of biotin-dependent acetyl-CoA carboxylase, a key enzyme in fatty acid biosynthesis; thereby, decreasing the synthesis of saturated fatty acids. Therefore, the ratio of unsaturated to saturated fatty acids in the membrane increases, leading to further fluid permeable membrane. These structural modifications increase the membrane permeability, facilitating the active and passive secretion of L-lysine into the extracellular media. This secretion is not merely a byproduct of leakage; it is a strategic requirement to decrease the intracellular concentration of lysine; thereby, decreasing residual feedback pressure on biosynthetic enzymes and preventing cellular toxicity.

5.3. Enzymatic Biocatalysis: a Precision Alternative

While fermentation is the primary production method, enzymatic synthesis offers a highly specific alternative, particularly for pharmaceutical uses where ultra-high purity is non-negotiable [25]. This approach typically involves the stereospecific conversion of chemical precursors, most significantly DL- α -amino- ϵ -caprolactam. The process uses a multiple-enzyme system of an α -amino- ϵ -caprolactam racemase that continuously interconverts the D and L-isomers of the precursor and an α -amino- ϵ -caprolactam hydrolase (lysine lactamase) that selectively opens the lactam ring of the L-isomer to yield L-lysine. The primary advantage of the enzymatic route includes its absolute stereoselectivity and the absence of the complex organic biomass in fermentation broths, which significantly simplifies the subsequent purification steps. Compared to simple sugars, the high cost of the caprolactam precursor often limits this method to high-value pharmaceutical grades rather than the bulk feed market.

5.4. The Failure of Traditional Chemical Synthesis

The historical roots of L-lysine production is linked to the total chemical synthesis, beginning with substrates such as cyclohexane, butadiene or caprolactam. These methods



generally involve multiple-step halogenation and amination reactions to form the diamino-acid backbone. However, chemical synthesis suffers from a fundamental defect for biological nutrition, as it is non-stereospecific. The resulting product is a racemic mixture (DL-lysine), containing equal parts of the biologically active L-isomer and the nutritionally inert D-isomer. Since animals and humans lack the racemases necessary to convert D-lysine into its usable L-form, half of the synthesized product is effectively wasted unless an expensive and labor-intensive resolution step (e.g., fractional crystallization or enzymatic resolution) is carried out. Furthermore, the reliance on petrochemical feedstocks and the generation of hazardous chemical waste makes this pathway environmentally and economically inferior to the green fermentation of renewable sugars. The economic viability of fermentation-based amino acid production using low-cost substrates such as molasses has been verified in multiple studies [23].

5.5. Downstream Processing: Recovery and Purification Architectures

The final phase of industrial production involves the extraction of L-lysine from the fermentation soup, which contains bacterial cells, residual nutrients and various metabolic byproducts [9]. This process, known as downstream processing, typically accounts for a significant portion of the total production cost.

1. Primary separation: The process begins with the removal of microbial biomass through high-speed centrifugation or ultrafiltration. In feed-grade operations, the entire broth (including the dead cell mass) is dried to

produce a lysine-rich biomass, but for crystalline products, a clear supernatant is needed.

2. Ion-exchange chromatography: This is the core purification step. Because L-lysine carries a net positive charge at acidic to neutral pH, the clarified broth is passed through columns packed with a strong acid cation-exchange resin. The lysine molecules are selectively adsorbed onto the resin, while neutral and acidic impurities pass through. The adsorbed L-lysine is then eluted using an alkaline solution, typically ammonia.

3. Concentration and acidification: The eluate is concentrated via multiple-effect vacuum evaporation. To improve stability and shelf life, hydrochloric acid is added to the concentrated solution to convert the free base lysine into L-lysine monohydrochloride (L-lysine HCl).

4. Crystallization and drying: The final product is crystallized through controlled cooling, separated by centrifugation and dried in fluidized-bed dryers. The resulting crystalline powder is a highly stable non-hygroscopic product ready for global distribution in the pharmaceutical and agricultural sectors.

6. FACTORS AFFECTING L-LYSINE YIELD

The industrial production of L-lysine through microbial fermentation is a complex process, where the final yield is governed by a delicate interplay between the environmental conditions and the genetic architecture of the producing strain (Table 4). Optimizing these factors is essential to maximize metabolic flux to lysine and ensure the economic viability of the bioprocess.

Table 4. Key regulatory factors in L-lysine fermentation

Factor	Role in Production	Industrial Strategy
Aspartokinase (AK)	Primary regulatory node; subject to concerted feedback inhibition	Use of regulatory mutants insensitive to feedback
Biotin (Vitamin B7)	Cofactor for pyruvate carboxylase; regulates membrane permeability	Control concentrations at sub-optimal levels to facilitate secretion
DHDPS	First committed enzyme of the lysine branch	Desensitize allosteric sites to prevent inhibition by rising lysine levels
Auxotrophy	Prevents carbon flux diversion to other pathways	Deploy threonine- or homoserine-auxotrophs to funnel precursors

6.1. Environmental Factors

The efficiency of L-lysine fermentation in bioreactors heavily depends on several physical and chemical parameters, including pH, temperature and dissolved oxygen levels. Maintaining an optimal pH is critical for

cellular homeostasis and enzyme activity; typically, pH and temperature must strictly be controlled throughout the batch or fed-batch process to support high growth rate and metabolic productivity. Aeration and agitation are equally vital, as L-lysine synthesis is a highly aerobic process. Sufficient oxygen levels (O₂) must be set to support the



oxidative metabolism of the carbon source, while agitation ensures the uniform distribution of nutrients and prevents the accumulation of inhibitory byproducts.

As detailed in Section 4.2, biotin concentration is a critical environmental parameter for *C. glutamicum* fermentation, as it affects anaplerotic carbon flux via pyruvate carboxylase and membrane permeability through its effects on fatty acid synthesis; thereby, affecting intracellular lysine accumulation and feedback regulation [24, 26]. Additionally, the concentration of growth factors such as L-homoserine, L-threonine and L-methionine must carefully be managed. These must be supplied to the media at levels less than the optimum for growth to prevent the activation of regulatory mechanisms that shut down lysine production.

6.2. Genetic Factors

The overproduction of L-lysine needs circumvention of the natural regulatory brakes within the microbial cell. In wild types, the lysine biosynthetic pathway is tightly regulated by the concerted feedback inhibition of the enzyme aspartokinase by L-lysine and L-threonine. To solve this problem, industrial strains are often engineered as auxotrophic mutants. For example, homoserine-auxotrophic mutants are commonly used because they cannot synthesize threonine or methionine. By limiting the supply of these amino acids in the media, the concerted inhibition of

aspartokinase is bypassed, allowing for the continuous flux of carbon toward lysine.

Furthermore, regulatory mutants are developed to provide resistance to lysine analogs such as S-(2-aminoethyl)-L-cysteine (AEC). These mutants possess a modified aspartokinase that is desensitized to feedback inhibition, ensuring that the enzyme is active even in the presence of high intracellular concentrations of L-lysine. Advanced genetic engineering techniques, including gene cloning and the optimization of promoter strength, are used to increase the expression of key enzymes such as pyruvate carboxylase and lysine permease (*lysA*), which facilitates the rapid transport of lysine out of the cell [27]. Recent developments involve metabolic engineering to redirect carbon flux from competing pathways such as the synthesis of isoleucine or methionine, further enhancing the specific productivity of the production strain.

7. DIVERSE USES OF L-LYSINE

The diverse uses of L-lysine span within multiple sectors, ranging from large-scale agricultural operations to specialized clinical pharmacology. Its status as an indispensable amino acid with its unique chemical reactivity, makes it a cornerstone in global nutrition and medicine. This section has provided an in-depth analysis of how L-lysine is used to optimize animal growth, improve human physiological outcomes and support the global food supply (Table 5).

Table 5. Various uses of L-lysine

Sector	Primary applications
Animal nutrition	First limiting amino acid in cereal-based diets for swine/poultry; decreases nitrogen excretion
Human health	Therapeutic agent against Herpes Simplex Virus (HSV); improves calcium absorption
Pharmacology	Formulation of IV solutions; counter-ion for drugs like ibuprofen to improve solubility
Neurobiology	Partial antagonist to serotonin (5-HT ₄) receptors; mitigates stress-induced anxiety
Food industry	Fortification of bread and flour in regions with protein-energy malnutrition

7.1. Animal Nutrition and Agricultural Economics

In the livestock industry, L-lysine is addressed as one of the most economically significant feed additives [28]. For monogastric animals, particularly swine and poultry, L-lysine is typically the first limiting amino acid in conventional corn and soybean meal-based diets. However, this generalization does not hold for all cereal sources. In wheat-based diets, threonine often becomes limiting whereas in rice-based diets, methionine or lysine may be co

-limiting depending on the specific formulation. The law of the minimum in nutrition dictates that protein synthesis is limited by the amino acid at the lowest concentration relative to the animal's requirement. Since cereal grains are naturally deficient in lysine, absence of supplementation leads to suboptimal nitrogen retention and stunted muscle development.

By incorporating crystalline L-lysine into feed formulations, nutritionists can significantly decrease the total crude protein content of the diet [29]. This allows for



the replacement of expensive high-protein components such as soybean meal with further cost-effective carbohydrate sources. In addition to simple growth promotion, L-lysine supplementation has profound environmental implications. When diets are balanced with precise amino acid profiles, the efficiency of protein use increases, which leads to a significant decrease in nitrogen excretion in animal waste. This mitigation is critical for reducing the environmental footprint of industrial farming, particularly in preventing the nitrogen loading of groundwater and soil.

7.2. Human Health and Clinical Pharmacology: Antiviral and Cardiovascular Roles

The clinical use of L-lysine is perhaps best documented in its role as a therapeutic agent against the HSV [30]. The biochemical basis for this use depends on the antagonistic relationship between L-lysine and L-arginine. The HSV replication highly depends on arginine-rich proteins; L-lysine acts as a competitive inhibitor for arginine transport within cellular membranes and competes for the same enzymatic pathways used in viral capsid assembly [7]. Clinical studies have demonstrated that high-dose L-lysine supplementation effectively shifts the lysine-to-arginine ratio in the plasma, leading to a significant decrease in the frequency, duration and severity of cold sore outbreaks.

In addition to its antiviral characteristics, L-lysine plays an emerging role in cardiovascular health and systemic detoxification. In addition to its role in carnitine synthesis, L-lysine has been investigated for its potential involvement in cardiovascular health, largely based on its theoretical ability to interfere with lipoprotein(a) [Lp(a)] deposition. However, clinical evidence supporting a direct artery-clearing effect in humans is limited and inconclusive. It acts as a precursor to carnitine, which facilitates fatty acid oxidation and is involved in the structural maintenance of the vascular wall. Clinical paradigms suggest that L-lysine, in combination with Vitamin C, may prevent the deposition of lipoprotein(a) in arterial walls; thereby, offering a protective mechanism against atherosclerosis and angina pectoris [5, 31]. Furthermore, its role in antibody production is fundamental to the adaptive immune system, where it provides the structural backbone for the hypervariable regions of immunoglobulins. Recent research on pulmonary toxicity has highlighted the importance of antioxidant and anti-inflammatory agents in protecting lung tissue against environmental toxicants, an area where L-lysine antioxidant characteristics may prove beneficial.

7.3. Bone Health, Osteoporosis Prevention and Calcium Homeostasis

A critical often overlooked use of L-lysine includes its profound effect on mineral metabolism, specifically Ca^{2+} homeostasis [32]. The L-lysine is essential for the intestinal absorption of calcium and, more importantly, for its renal conservation. By enhancing the efficiency of calcium uptake and decreasing its excretion in urine, L-lysine ensures that a higher concentration of the mineral is available for incorporation into the hydroxyapatite matrix of the bone. This makes it a vital nutritional intervention for the prevention and adjunct treatment of osteoporosis, particularly in post-menopausal women and elderly populations. Moreover, the role of L-lysine in the cross-linking of collagen fibers is essential for bone quality rather than density alone [33]. While calcium provides hardness, the lysine-derived collagen cross-links provide the tensile strength and flexibility that prevent fractures. Without adequate lysine-mediated hydroxylation and cross-linking (catalyzed by lysyl oxidase), the bone matrix becomes fragile, regardless of the mineral content.

7.4. Neuropharmacology and Anxiety Decrease

Recent advancements in neurobiology have identified L-lysine as a potent modulator of the central nervous system (CNS). Specifically, L-lysine has been shown to act as a partial antagonist to serotonin receptors (5-HT₄) in the gut and brain [34]. Chronic deficiency in L-lysine has been correlated to increased pathological anxiety and increased levels of stress-induced cortisol. Clinical trials involving populations with cereal-based, lysine-poor diets have demonstrated that fortification with L-lysine can significantly decrease reported levels of anxiety and modulate the body's physiological response to stress. This nutritional neurobiology approach offers a non-pharmacological pathway to managing subclinical anxiety through dietary optimization.

7.5. The Food Industry and Nutritional Fortification

The global food industry uses L-lysine to address the cereal gap in human nutrition. In several developing regions, the primary caloric intake is derived from wheat, rice and/or maize, all of which are deficient in L-lysine. This deficiency contributes to a cycle of protein-energy malnutrition (PEM), characterized by impaired growth and



weakened immunity in children [35]. To combat this, L-lysine is used to fortify flours, breads and specialized infant formulas. In addition to basic fortification, L-lysine is used as a functional ingredient in the pharmaceutical industry to improve the pharmacological profile of drugs. For example, lysine ibuprofenate is a common formulation, where L-lysine is used as a counter-ion to increase the solubility and absorption rate of the analgesic, leading to a faster onset of action [11]. In the cosmetic industry, L-lysine role in collagen synthesis is leveraged in topical creams designed to promote wound healing and skin elasticity.

7.6. Emerging Frontiers: cancer Immunotherapy and Metabolic Reprogramming

Cutting-edge research suggests that lysine metabolism is intimately linked to tumor biology and immune evasion [36]. Lysine catabolism has been reported to reprogram tumor immunity through a process called histone crotonylation [37]. By modulating the breakdown of lysine within the tumor microenvironment, researchers investigate ways to unmask cancer cells to the immune system. This suggests that L-lysine levels or its metabolic enzymes can be targeted as part of a comprehensive cancer immunotherapy strategy, moving the use of this amino acid from simple nutrition to high-precision oncology.

8. RECENT ADVANCES AND FUTURE PERSPECTIVES

The biotechnological landscape of L-lysine production is currently undergoing a paradigm shift, driven by the convergence of synthetic biology, systems metabolic engineering and global imperative for circular bioeconomies. As the industrial demand for this essential amino acid (EAA) scales to unprecedented volumes, researchers move to precision genome editing and use of non-conventional carbon feedstocks in addition to classical mutagenesis. This section has delineated the recent breakthroughs that are redefining efficiency, sustainability and economic viability of L-lysine manufacturing.

8.1. Precision Metabolic Engineering and Synthetic Biology

The most significant recent advances in L-lysine production originate from the use of CRISPR/Cas9 and CRISPRi (interference) technologies in *C. glutamicum* [38]. Traditional strain development depends on random mutagenesis, which often introduced deleterious secondary

mutations. Modern metabolic engineering allows for the site-specific fine-tuning of the entire DAP pathway. In addition to merely desensitizing aspartokinase to feedback inhibition, scientists are focusing on metabolic flux analysis (MFA) to identify hidden bottlenecks. For example, recent studies have targeted the pentose phosphate pathway (PPP) to increase the intracellular supply of NADPH, the primary reducing equivalent needed for the high-yield conversion of precursors to lysine [39]. By overexpressing glucose-6-phosphate dehydrogenase (G6PD) and simultaneously deleting competing pathways (e.g., those leading to lactic acid or acetic acid formation), researchers have achieved zero-byproduct fermentation, where nearly every gram of glucose is converted into lysine or essential biomass.

Furthermore, the engineering of efflux transporters has emerged as a critical frontier. The LysE protein acts as a specific exporter that pumps L-lysine out of the cytoplasm [40]. Recent advances involve increasing the copy number of the *lysE* gene or engineering its promoter to ensure that as soon as lysine is synthesized, it is immediately expelled into the extracellular broth. This rapid transport not only simplifies downstream recovery but also keeps the intracellular lysine concentration less than the threshold that triggers arene homeostatic repression mechanisms.

8.2. Sustainable Production and the Circular Bioeconomy

As global industries transition away from food-competitive feedstocks (e.g., pure glucose and cane sugar), use of agricultural and industrial waste as a substrate has become a primary focus. This second-generation (2G) biorefining approach aims to produce L-lysine from lignocellulosic biomass such as corn Stover, wheat straw and waste gases.

- **Lignocellulosic substrates:** Recent research has focused on engineering to co-use xylose and arabinose (the primary sugars in hemicellulose) with glucose [41]. Naturally, several industrial strains prefer glucose and demonstrate carbon catabolite repression against other sugars. By deleting the genes responsible for this repression and introducing heterologous transporters, researchers have successfully converted agricultural residues into high-value L-lysine, effectively decoupling amino acid production from the human food chain.

- **Waste-to-value paradigms:** Innovative studies have investigated use of crude glycerol (a byproduct of biodiesel production) and methanol as alternative carbon sources.



Development of methylotrophic strains represents a radical shift to a C1-based bioeconomy, where greenhouse gases or their derivatives can biologically be sequestered and transformed into essential nutrients [42].

8.3. Integration of Omics and Digital Twins in Bioprocessing

The future of L-lysine production is increasingly tied to the integration of omics technologies (genomics, transcriptomics and proteomics) and artificial intelligence (AI). Recent reviews have systematically investigated transformative role of omics technologies and digital twin technologies in advancing fermentation science [43]. By collecting large datasets from real-time fermentation runs, industrial producers are developing digital twins, virtual replicas of physical bioreactors that leverage real-time data and advanced algorithms to simulate, optimize and control fermentation processes [44]. The successful implementation of digital twins in bioprocessing offers numerous advantages, including enhanced understanding of processes, accelerated development timelines and effective monitoring of critical process parameters.

These AI-driven models can predict optimal feeding strategies and process outcomes. For example, deep learning-assisted media design has successfully been used to improve cell productivity of *C. glutamicum*, achieving high specific growth rates through deep neural network (DNN)-assisted optimization with Bayesian optimization and genetic algorithms [45]. Machine learning models, including convolutional neural networks (CNN) and long short-term memory (LSTM) networks, have been used for real-time bioprocess control and prediction of fermentation trajectories. Digital twins and soft-sensing technologies enable real-time control and increase operational precision in complex bioprocess environments [46].

This level of precision facilitates the transition from traditional batch fermentation to further efficient modes such as continuous or repeated-batch fermentation. Recent studies have demonstrated the potential of biofilm-based continuous fermentation for L-lysine production using engineered *C. glutamicum* strains [47]. For example, an elongated *C. glutamicum* strain constructed by downregulating the cell division gene of *ftsZ* achieved an average L-lysine titer of 143.3 g l⁻¹ with a yield of 66.4% (lysine/glucose) during continuous fermentation; a 6.8%

improvement compared to the wild-type strain. Another study showed that heterologous expression of the *csIA* gene increased biofilm formation by 135% and resulted in an average of 26.1% higher L-lysine production, compared to the wild-type strain in biofilm-based continuous fermentation [48]. These approaches offer advantages such as enhanced cell stability, prolonged metabolic activity and resistance to environmental stress, ultimately increasing volumetric productivity (g l⁻¹ h⁻¹) and decreasing operational downtime.

8.4. Future Prospects: Beyond Nutrition

Looking forward, the scope of L-lysine uses is expected to expand into the advanced materials and precision medicine [10]. The development of lysine-based polymers (poly-lysine) for drug delivery systems and biodegradable plastics is an area of intense research. Furthermore, as the current understanding of the lysine catabolism-cancer axis matures—particularly the role of lysine in histone crotonylation and tumor immunity—the production of specialized L-lysine isotopes or derivatives for oncological diagnostic imaging and targeted therapy may become a high-value niche in the pharmaceutical market.

9. CRITICAL APPRAISAL AND RESEARCH GAPS

Despite the extensive body of literature on L-lysine, several contradictory findings and methodological limitations warrant critical discussion. For example, while numerous clinical studies support the efficacy of L-lysine supplementation in decreasing HSV recurrence, other randomized controlled trials (RCT) have reported only marginal benefits, suggesting that the therapeutic outcome may highly be dependent on individual baseline lysine-to-arginine ratios, dose regimens and viral strain variability. For industrial production, although metabolic engineering has dramatically improved yields, the transition from laboratory-scale to commercial-scale bioreactors often reveals unforeseen bottlenecks such as oxygen transfer limitations and accumulation of inhibitory byproducts, which are rarely addressed in published strain development studies. Furthermore, the long-term stability of L-lysine in functional foods and animal feed pellets is an understudied area, particularly regarding the Maillard reaction kinetics under various processing conditions. The emerging role of lysine metabolism in cancer immunotherapy is still in its



infancy and most evidence relies on preclinical models; large-scale human translational studies are urgently needed to validate these findings. Addressing these gaps through interdisciplinary research is critical for unlocking the full potential of L-lysine in clinical and industrial settings.

10. CONCLUSION

This review has highlighted L-lysine as a critical intersection of biochemistry, industrial biotechnology and clinical medicine. Its unique structure underpins essential roles in protein synthesis, collagen cross-linking and metabolic regulation, while the evolutionary divergence of its biosynthetic pathways (DAP in bacteria/plants and AAA in fungi) has enabled sophisticated metabolic engineering for industrial production. Through *C. glutamicum* fermentation, the industry achieves high yields by circumventing regulatory inhibitions and optimizing parameters such as biotin levels, with global production exceeding 1 million metric tons annually. In addition to animal nutrition, L-lysine demonstrates therapeutic promise in antiviral therapy, bone health, neuropharmacology and emerging roles in cancer immunotherapy. Recent advances in CRISPR-based genome editing, omics integration and AI-driven bioprocess optimization are providing a way for sustainable waste-to-value production. However, challenges include Maillard reaction susceptibility in feed processing and need of efficient racemic resolution in alternative syntheses. Ultimately, interdisciplinary collaboration is essential to unlock the full potential of L-lysine in promoting human health, sustainable agriculture and global bioeconomy.

11. DECLARATION STATEMENTS

11.1. Conflict of interest

The authors declare no conflict of interest.

11.2. Authors' contributions

H.A., Conceptualization, investigation, writing-original draft, visualization; J.F., conceptualization, supervision, project administration, writing-review and editing, validation. All authors have read and approved the final version of the manuscript.

11.3. Use of artificial intelligence (AI) chatbots

During the preparation of this study, the authors used Grammarly for language editing and readability enhancement. No AI tools were used for data analysis, interpretation or generation of scientific content. The authors take full responsibility for the originality, accuracy and integrity of the manuscript.

11.4. Ethical consideration

This study was a literature review and did not involve human participants, animal subjects or experimental procedures needing ethical approval.

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ال-لیزین: مروری جامع بر مسیرهای بیوسنتز، روش‌های تولید صنعتی و کاربردهای متنوع

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چکیده

سابقه و هدف: ال-لیزین، یک اسید آمینه ضروری، نقش‌های کلیدی در سنتز پروتئین، تنظیم متابولیک و یکپارچگی ساختاری ایفا می‌کند. این مقاله مروری، نمای کلی گسترده‌ای از ویژگی‌های شیمیایی، مسیرهای زیست‌ساخت، راهبردهای تولید صنعتی و کاربردهای متنوع ال-لیزین در حوزه‌های تغذیه، پزشکی و زیست‌فناوری ارائه می‌دهد.

روش راهبرد جستجوی منابع: جستجوی نظام‌مند در پایگاه‌های PubMed، Scopus و Web of Science تا آخر سال ۲۰۲۵ انجام شد. کلیدواژه‌های مورد استفاده شامل ال-لیزین، زیست‌ساخت، تخمیر، کورینه‌باکتریوم گلوتامیکوم و کاربردها بودند. مقالات پژوهشی اصیل، مقاله‌های مروری و ثبت‌اختراعات مرتبط از مراجع معتبر بین‌المللی مانند USPTO، WIPO و EPO به‌دقت ارزیابی شدند. از آنجا که این مطالعه یک مرور روایتی است، تمرکز بر ارائه‌ی یک نمای کلی از حوزه‌ی موردنظر بوده و نه یک فراتحلیل کمی بود.

یافته‌ها و نتیجه‌گیری: مسیر دی‌آمینوپیملیک اسید (DAP) در باکتری‌ها و گیاهان و مسیر آلفا-آمینوآدیپیک اسید (AAA) در قارچ‌ها به‌طور مشروح تشریح شده‌اند. تولید صنعتی بر پایه‌ی سویه‌های مهندسی‌شده‌ی کورینه‌باکتریوم گلوتامیکوم دارای آسپاراتوکیناز مقاوم به بازخورد، سطوح بهینه‌شده‌ی بیوتین و فرآیند پایین‌دستی خالص‌سازی با کروماتوگرافی تبادل یونی استوار است. کاربردهای کلیدی شامل مکمل‌سازی خوراک دام، درمان ضدویروسی (عفونت‌های هرپس سیمپلکس)، سلامت استخوان، کاهش اضطراب و نقش‌های نوظهور در ایمونوتراپی سرطان می‌شود. همچنین پیشرفت‌های اخیر در فناوری CRISPR/Cas9، تحلیل شار متابولیک و استفاده از خوراک‌های پایدار برجسته شده‌اند. ال-لیزین یکی از ارکان اقتصاد زیستی جهانی با کاربردهای رو به گسترش در حوزه‌های دارویی و مواد مهندسی است. مهندسی متابولیک دقیق و رویکردهای اقتصاد زیستی چرخشی، نوآوری‌های آینده را در این زمینه هدایت خواهند کرد.

واژگان کلیدی: کاربردها، زیست‌ساخت، کورینه‌باکتریوم گلوتامیکوم، تولید صنعتی، ال-لیزین