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The Development of Low-Purine Soy Products and Their Bioinformatics-Driven Optimization

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Abstract. Hyperuricemia and gout are linked to imbalances in purine metabolism and uric acid excretion. Soy, a high-quality plant protein with moderate purine content, generally has limited impact on serum urate, but low-purine products are still needed for high-risk groups. Since purines migrate and transform during processing such as soaking, grinding, heating, and fermentation, processing becomes a key factor in controlling purine levels. This paper examines the release, transformation, and removal of purines in soy and presents processing strategies and intelligent optimization for developing low-purine soy products. As such, this paper reviews the metabolism and processing of purines in soy and, through mechanistic analysis, investigates their migration and degradation. Moreover, it evaluates raw material selection and processing steps, explores digital twins, predictive models, multi-omics, and enzyme engineering for optimizing low-purine processing, and assesses the feasibility and standards of these products for production, quality, regulations, and sensory attributes. Taken together, evidence indicates that appropriate processing can lower purine content, and that bioinformatics-enabled control improves consistency and scale-up feasibility.

Keywords: Low-Purine Foods, Soy Products, Purine Metabolism, Bioinformatics

1. Introduction

Hyperuricemia and gout are primarily caused by imbalances in purine metabolism and uric acid excretion. As humans lack uricase, dietary purines play a major role in determining serum urate levels, highlighting the importance of dietary management in non-pharmacological strategies [1,2]. Although soy foods offer high-quality protein, bioactive compounds, and environmental benefits, their moderate purine content may cause concern for individuals at high risk of gout. Prior studies have shown that moderate soy consumption typically exerts only a modest influence on serum urate levels [1,3]. However, low-purine labels need standard testing and process control to gain trust and ensure safe intake for at-risk groups. In soy processing, purines may enter water during soaking, grinding, and heating, and be altered by microbes or enzymes or removed through adsorption and membranes [4,5]. With the development of bioinformatics and artificial intelligence tools such as multi-omics analysis, data-driven parameter estimation, and digital twin modeling, it is now feasible to design bioprocesses predictively rather than relying on trial-and-error [6,7]. This paper reviews the latest studies on purine regulation in soy, presents a comprehensive framework covering raw material selection, pretreatment, fermentation, enzymatic conversion, as well as separation, and

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investigates the role of bioinformatics in optimizing each step. Moreover, it highlights measurement standards, scale-up challenges, and regulatory and sensory barriers as key obstacles while stressing priorities for translating laboratory results into commercial production.

2. Risk of high-purine diets and purine metabolism characteristics of soy

2.1. High-purine diets and the mechanism of gout

Elevated serum urate levels, frequently caused by a diet rich in purines, represent a major risk factor for gout [2,3,8]. Besides, both dietary and endogenous purines contribute to urate production. In the intestine, nucleotides are dephosphorylated into nucleosides and absorbed via specific transporters. Thereafter, in the liver, purine bases can be recycled through salvage pathways to produce inosine monophosphate (IMP), adenosine monophosphate (AMP), and guanosine monophosphate (GMP). If salvage pathways are limited, nucleosides are converted into hypoxanthine and guanine, which are subsequently oxidized to uric acid by xanthine oxidoreductase. In humans, the lack of uricase renders uric acid the end product of purine metabolism. When its concentration exceeds solubility (~6.8 mg/dL), monosodium urate crystals form, activating the NLRP3 inflammasome and triggering IL-1β-mediated inflammation, leading to gout attacks [2]. Urate levels are regulated by the balance between synthesis and excretion: the kidney reabsorbs urate via URAT1 and GLUT9 and secretes it through organic anion transporters (OATs), while the intestine contributes via ATP-binding cassette subfamily G member 2 (ABCG2). In addition, dietary and lifestyle factors strongly influence this balance. Fructose and ethanol tend to increase serum urate levels, whereas sufficient hydration, vitamin C, and low-fat dairy intake facilitate urate excretion [8,9]. Besides, food matrix and gut microbiota also affect absorption; water-soluble nucleosides are more bioavailable than polymeric nucleic acids, and intestinal microbes can partially degrade purines, reducing their uptake [3].

2.2. Purine characteristics of soy and metabolic regulation

Higher in purines than most cereals, soy provides around 130~150 mg per 100 g, thus placing it at a moderate level among legumes [10]. As precursors of uric acid, purines are closely associated with hyperuricemia and related metabolic disorders, highlighting the importance of monitoring their levels and changes during processing for dietary health. In soy, purines are primarily adenine- and guanine-derived nucleotides and nucleosides, with lower levels of hypoxanthine and xanthine. And these water-soluble compounds are prone to migration during processing, with soaking causing partial leaching of purines into the liquid, while wet grinding and heating disrupt cell structures and enhance their diffusion into the aqueous phase. Thus, discarding the soaking liquid at this stage can effectively reduce residual purines. Purine concentration is strongly influenced by water content and protein aggregation. Consequently, during coagulation and tofu formation, water is expelled and proteins are concentrated, which increases the apparent purine levels on a wet basis, while some purines simultaneously migrate into the whey. Pressing, dewatering, and drying further concentrate remaining purines, whereas clarification, membrane filtration, or centrifugation remove the soluble fraction, lowering total purine content. Moreover, purine release and reconcentration are affected by factors such as seed-coat permeability, cell-wall integrity, dehulling, soybean variety, particle size, pH, ionic strength, and germination status. To reduce purines, processing strategies emphasize early release and removal of soluble purines via blanching, filtration, or microbial/enzymatic treatment before coagulation, while retaining key nutrients [4].

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2.3. Low-purine requirements and industrial applications

Given that adherence to strict low-purine diets is often low, the food industry faces an urgent need to produce everyday foods with naturally reduced purine content that do not require consumers to follow rigid restrictions [4]. However, clearly labeled low-purine soy products are still scarce, and inconsistent analytical standards and labeling practices not only limit their clinical application but also affect consumer trust [4]. Although moderate soy intake usually has only a modest effect on serum urate levels, for high-risk or sensitive populations, low-purine versions of staple soy foods remain beneficial; thus, the development of targeted low-purine soy products is still necessary [1,3]. In industrial applications, several strategies can be adopted to reduce purine content in soy products. These strategies begin with raw material selection and pretreatment, followed by early removal of soluble purines through discarding soaking or whey liquids. To further lower purines, soy products may be treated via biotransformation using nucleotidases, nucleoside phosphorylases, deaminases, or starter cultures, along with optimized coagulation and dewatering to minimize reconcentration of purines. In industrial production, it is crucial to implement rapid or in-line purine testing, uphold batch-to-batch uniformity, retain flavor and texture, adhere to regulatory and allergen requirements, and maintain cost-effectiveness. Notably, existing patents and pilot-scale processes provide feasible pathways for large-scale production [11]. Amid pressures of sustainable plant protein and purine control, low-purine soy products offer opportunities for industrial innovation while also supporting health, flavor, safety, and cost efficiency.

3. Key process pathways for reducing purine content in soy products

3.1. Raw material selection and pretreatment techniques

The reduction of purine content in soy begins with raw material selection and pretreatment, which lay the foundation for further processing. Equally important is the choice of low-purine cultivars. Due to the significant differences in purine content across soybean varieties, opting for low-purine cultivars can substantially decrease the initial purine load, hence managing purine levels from the beginning. In terms of pretreatment techniques, dehulling, sprouting, and soaking constitute the primary methods. Dehulling removes the seed coat, which hinders purine diffusion; after dehulling, water penetrates better, helping extract soluble purines during later wet processing. This step raises handling costs but minimally influences sensory quality. In addition, sprouting induces endogenous turnover of nucleosides and nucleotides to support ribonucleotide synthesis, decreasing free purine levels. Its effectiveness depends on germination time and requires strict microbial control to ensure safety. Soaking is the most common pretreatment in soy milk and tofu production, as immersing soybeans in clean water for several hours can remove a large portion of soluble purines. It should be noted that higher soaking temperatures accelerate purine diffusion and may also increase nutrient loss and contamination risk. Thus, optimal time and temperature should be combined with correct water-to-bean ratios, sanitation, and rapid cooling, while coarse grinding before soaking can boost mass transfer but may cause some solid loss. This indicates that selecting low-purine cultivars along with carefully managed dehulling, sprouting, and soaking can significantly reduce the initial purine content and create favorable conditions for subsequent processing, with temperature, duration, and microbial control being crucial to ensure the pretreatment is both effective and safe [4].

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3.2. Fermentation processes and strain optimization techniques

Fermentation not only reduces purine content in soy but improves flavor and texture, making it a crucial method for producing low-purine soy products. For example, traditional fermented products like douchi, miso, and natto partially degrade nucleic acids and nucleosides under microbial activity, resulting in lower purine levels than in unfermented soy. Furthermore, fermentation effectiveness depends on key enzymes, including adenosine deaminase (ADA), guanine deaminase (GDA), and purine nucleoside phosphorylase (PNP), which are mainly from safe lactic acid bacteria, food-grade molds, and selected yeasts. These enzymes convert adenosine, guanosine, and inosine into poorly absorbed or removable compounds, lowering purine levels. Meanwhile, fermentation performance is strongly influenced by substrate form, temperature, pH, salinity, aeration, moisture, and nutrient balance. Under conditions that avoid inhibitory interactions, co-culture systems can simultaneously enhance flavor development and purine conversion. Besides, in-process monitoring of nucleosides and purine bases enables adaptive control and maintains batch-to-batch consistency. As such, strain selection and process optimization are key to reducing purines during fermentation. By carefully designing strain combinations and strictly controlling fermentation conditions, purine levels can be reliably reduced while keeping flavor and sensory quality [12,13].

3.3. Enzymatic degradation and process integration

Enzymatic treatment enables rapid, targeted reduction of purines and ensures predictable outcomes within a short time. The process usually involves two steps: nucleases degrade DNA and RNA into oligomers and nucleosides, followed by ADA, GDA, and PNP, which convert these intermediates into less bioavailable or more easily removed compounds. Furthermore, enzymatic methods are applied across diverse contexts, including bench-scale in vitro systems, enzyme-assisted soy milk processing, and engineered yeasts expressing deaminases. Insights from low-purine beer production highlight the effectiveness of exogenous PNP in reducing nucleoside levels. In addition, integration with unit operations enhances efficiency. Enzyme addition during or after wet grinding improves substrate accessibility, while coupling enzymatic steps with clarification, membrane separation, or food-grade adsorbents allow soluble products to be removed before coagulation concentrates them. Cost and stability can be boosted via GRAS-approved enzyme sources, enzyme immobilization, and protection from heat or shear stress. Sensory risks can be minimized by adjusting enzyme dosage, controlling reaction time, and promptly removing by-products. Consequently, enzymatic conversion can markedly reduce purines within short processing times, particularly when coordinated with liquid-phase separation, cost control, stability management, and flavor preservation. Optimal results require integration of enzymatic steps with overall process design [5,6,12].

3.4. Adsorptive removal and physical field intensification

Adsorptive and physical methods act as complementary strategies for purine reduction, reinforcing enzymatic and microbial treatments. Typical adsorbents such as activated carbon, zeolites, and chitosan capture purines from aqueous systems but may strip flavors, vitamins, and peptides [14]. Their efficiency depends on material type, pore structure, and contact time, all of which require careful optimization to maintain selectivity. Besides, chemical precipitation and salting-out lower soluble purines but risk protein denaturation, off-flavors, and reagent residues, limiting industrial application. By disrupting cell walls, enhancing mass transfer, and driving early purine release into discardable streams, pulsed electric fields, high heat, ultrasound, and microwave treatments act as

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effective physical field techniques during soaking or blanching. Despite their effectiveness, energy demand, equipment needs, and impacts on texture and nutrients must be considered. Therefore, adsorptive and physical methods are best used as pretreatment or polishing steps after enzymatic or microbial conversion, when purines are soluble and easily separable. The effects on flavor, texture, nutrients, energy, and water use should be assessed to ensure feasibility. As part of multi-stage liquid-phase separation, these methods can further improve purine removal efficiency [4,11].

4. Integrated application of bioinformatics in process engineering

4.1. Intelligent prediction and digital twin process simulation

Deep learning combined with plant data enables monitoring and control of purine concentrations as measurable variables. When supplied with inputs like temperature, pH, dissolved oxygen, agitation, near-infrared spectra, and LC-MS readings, time-series models (such as LSTM, temporal CNN, Transformer) act as soft sensors, producing short-term forecasts with quantified uncertainty. When embedded in predictive controllers, these models guide operational targets to maximize purine removal while preserving yield, product quality, and energy efficiency [7]. Moreover, a digital twin reproduces fermenters or enzymatic units via three layers: data with real-time and historical streams, models with mechanistic and statistical approaches, and control with optimization and actuation. This structure enables closed-loop simulation, real-time adjustment, and on-the-fly recalibration [6]. In addition, purine bases can self-assemble at liquid-solid interfaces into G-quadruplex structures that are sensitive to temperature and metal ions [15]. Electrochemical and optical probes exploiting these interactions enable in-situ monitoring. When integrated into the digital twin, such sensor signals correct drift, detect anomalies, and guide material selection, improving detection stability and process control [16]. These advances highlight how predictive modeling, digital simulation, and advanced sensing converge to enable reliable purine management in industrial production.

4.2. Multi-omics and metabolic network modeling

Multi-omics methods enable systematic mapping of purine dynamics in soy matrices and microbial systems during processing. For instance, metabolomics across cultivars and pretreatments reveals shifts in nucleosides and bases during soaking, dehulling, and sprouting. Likewise, time-resolved transcriptomics and proteomics during fermentation capture the expression of ADA, GDA, PNP, and related transporters, directly linking enzyme activity with purine turnover. Moreover, kinetic and genome-scale metabolic models help identify rate-limiting steps and alternative pathways that may constrain reduction efficiency. In addition to process characterization, clinical relevance can be advanced by integrating animal and human datasets. In hyperuricemia models, urate burden and tissue injury correlate with inflammatory markers, including IL-6, IL-1β, CCL2, CCL5, CXCL10, STAT3, and TNF-α [2,17]. The incorporation of these signatures into network models could help link processing parameters with inflammatory risk. In population cohorts, network analysis and sparse regression reduce complex purine-pathway gene sets to predictive hubs for immune activity and enrichment outcomes [18]. This workflow supports fermentation design and informs personalized nutrition strategies.

4.3. Enzyme function prediction and structural engineering

The reduction of purine levels under mild, food-grade conditions depends on enzymes that are both stable and efficient. To this end, protein-language models combined with AlphaFold or ESMFold

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structural predictions and graph neural networks can classify enzyme families, define substrate ranges, and identify active-site residues. Through these approaches, high-throughput discovery of enzymes like PNP, ADA, GDA, uricase, and nucleases becomes possible from metagenomes and starter culture genomes. Furthermore, structural saliency maps guide targeted mutagenesis, while also docking and molecular-dynamics simulations facilitate screening of promising variants before experimental validation. Moreover, process outcomes depend on expression control in production strains, where predictive tools for post-transcriptional modifications such as m6A and m7G identify regulatory checkpoints that can be fine-tuned through promoter or UTR design and cultivation adjustments [19]. In parallel, enzyme immobilization, protective co-formulation, and operation under mild pH and temperature conditions can enhance stability and cost-efficiency, while minimizing sensory impacts [20,21].

4.4. Personalized nutrition and intelligent recommendation systems

At the consumer level, personalized systems help reduce purine intake without rigid diets. Hybrid recommenders integrating urate trends, genetic variants, microbiome profiles, medication use, and dietary logs generate tailored plans for low-purine soy products, with thresholds adjusted under conditions like dehydration, exercise, or alcohol consumption. To ensure follow-through and impact, wearable devices and home urate monitors supply real-time feedback on behavior and outcomes, which allows continuous model refinement. These digital phenotypes, combined with immune and purine-pathway biomarkers, can further support adaptive updates to dietary recommendations and product matching. At the production stage, aggregated consumer data feed into process design, with insights from recommendation systems guiding enzyme dosing, fermentation timing, and separation settings in the digital twin framework, thereby matching product profiles to real-world urate control needs [22]. From soft-sensor prediction and multi-omics modeling to enzyme engineering and personalized nutrition, these integrated approaches support a closed-loop framework that maximizes purine reduction while safeguarding product quality, safety, and scalability.

5. Future trends and challenges

The future development of low-purine soy products will therefore depend on holistic, intelligent design rather than isolated process improvements. Since single steps cannot simultaneously ensure health, flavor, nutrition, and cost-effectiveness, outcomes instead depend on coordinated control of purine release, transformation, and removal. In this context, data-driven and digital tools enhance process stability by integrating historical records, online spectroscopy, quality testing, and omics data with real-time prediction and virtual modeling, enabling tighter control and rapid correction reducing the need for frequent redesign [4-6,11].

Biotechnology and enzyme engineering provide the strongest potential for purine reduction under mild, food-grade conditions. Accordingly, future studies will emphasize discovering enzymes with broader substrate ranges and greater stability, developing microbial consortia that couple purine conversion with flavor formation, and designing metabolic routes that redirect nucleotides and nucleosides into removable or less absorbable products. To translate these advances into practice, technologies must be integrated with process equipment through optimized contact design, residence time control, and strategic separation layouts, while also safeguarding nutrition, flavor, and microbial safety. Furthermore, early-stage design should embed green and resource-efficient measures, such as lowering water and energy use, applying recyclable adsorbents, and immobilizing enzymes, to achieve sustainable processing [1,6,17,20].

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However, scaling up from laboratory to industrial production remains a major challenge. During this transition, gradient effects, contamination buildup, and cost pressures may arise, undermining laboratory outcomes. Therefore, validating robustness, capacity, and cost-effectiveness is essential in pilot and commercial stages. At the same time, standardizing data, methods, and models, through unified purine metrics, interoperable metadata, shared benchmarks, and clear model management, will enable reuse across factories and research groups. Looking ahead, the most promising path is a systematic approach that integrates multi-objective optimization of purine control, nutrition, flavor, safety, and environmental impact, while also establishing transparent performance indicators and lifecycle management. In this way, low-purine soy products can be developed that are clinically relevant, sensorially acceptable, and economically sustainable [4,19].

6. Conclusion

This review indicates that the efficient production of low-purine soy products relies on an integrated, mechanism-guided processing strategy rather than a single technological intervention. In particular, the process begins with the removal of soluble purines via aqueous extraction, followed by targeted bioconversion of bound purines, and prompt liquid separation to avoid purine buildup. Throughout this process, data-driven monitoring and control ensure stability. Meanwhile, bioinformatics plays a crucial role at each stage, enabling the prediction of key parameters, identification of bottlenecks, selection of appropriate enzymes and microbial strains, and optimization of the process based on end-point feedback. This approach allows low-purine products to retain nutrition, flavor, safety, and affordability. However, current research still has certain limitations. Experimental methods vary, most studies remain at the laboratory scale, and there is a lack of standardized purine measurement metrics and systematic comparative studies, which restricts the generalizability of results and their application across different production settings. Future research could develop standard tests and metadata, expand digital twin technologies from pilot to full-scale production, build libraries of mild-condition enzymes and microbial strains, and carry out prospective validation trials that link product performance with serum urate levels, cost, and environmental metrics. These efforts would enable sustainable low-purine soy processing across different production settings and populations.

References

[1] Duan, Y., Qi, Q., Liu, Z., Zhang, M., & Liu, H. (2022). Soy consumption and serum uric acid levels: A systematic review and meta-analysis. Frontiers in Nutrition, 9, 975718.
[2] Dalbeth, N., Choi, H. K., Joosten, L. A. B., et al. (2019). Gout. Nature Reviews Disease Primers, 5, 69.
[3] Messina, M., Messina, V. L., & Chan, P. (2011). Soyfoods, hyperuricemia and gout: A review of the epidemiologic and clinical data. Asia Pacific Journal of Clinical Nutrition, 20(3), 347-358.
[4] Zheng, Y., Ma, X., Li, L., et al. (2025). Purine content of different soybean products and dynamic transfer in food processing techniques. Food Chemistry: X, 28, 1002499.
[5] Shi, P., Zhang, R., Liu, C. X., et al. (2022). Computer-assisted in vitro reconstitution of the purine degradation pathway to lower the purine content in food. Journal of the Science of Food and Agriculture, 102(15), 7079-7086.
[6] Xia, J., et al. (2025). Optimization of fermentation processes in intelligent biomanufacturing: On online monitoring, artificial intelligence, and digital twin technologies. Chinese Journal of Biotechnology, 41(3), 1179-1196.
[7] Kwon, H. J., Shiu, J. H., & Yamakawa, C. K. (2024). Enhancing fermentation process monitoring through data-driven modeling and synthetic time series generation. Bioengineering, 11(8), 803.
[8] Maiuolo, J., et al. (2016). Regulation of uric acid metabolism and excretion. International Journal of Cardiology, 213, 8-14.
[9] Bobulescu, I. A., & Moe, O. W. (2020). Renal transport of urate. Kidney Research and Clinical Practice, 39(6), 491-510.

DOI: 10.54254/2753-8818/2025.AU28771

[10] Kaneko, K., et al. (2014). Total purine and purine base content of common foodstuffs. Biological & Pharmaceutical Bulletin, 37(5), 709-721.
[11] CN107691986B. (2021). Method for reducing the purine content of whole-grain soybean. China Patent.
[12] Liu, J., & Lu, J. (2025). Strategies for reducing purine accumulation in beer: From metabolic mechanisms to brewing technology innovations. Fermentation, 11(4), 193.
[13] Li, M., Yang, D., Mei, L., et al. (2014). Screening and characterization of purine nucleoside-degrading lactic acid bacteria from Chinese sauerkraut and evaluation of the serum uric acid-lowering effect in hyperuricemic rats. PLoS ONE, 9(8), e105577.
[14] Almeida, C., Neves, M. C., & Freire, M. G. (2021). Towards the use of adsorption methods for the removal of purines from beer. Molecules, 26(21), 6460.
[15] Chiorcea-Paquim, A. M., Eritja, R., & Oliveira-Brett, A. M. (2018). Electrochemical and AFM characterization of G-quadruplex electrochemical biosensors and applications. Journal of Nucleic Acids, 2018, 5307106.
[16] Li, Y. (2023). Assembly and regulation of interfacial structures of guanine and cytosine bioinformation molecules. Nanchang Institute of Technology.
[17] Miao, S. (2023). Bioinformatics-based gene analysis of chronic renal injury induced by hyperuricemia. Jilin University.
[18] Xu, T. (2024). Application of bioinformatics and machine learning in screening and validating purine metabolism-related genes and immunotherapy in coronary atherosclerosis patients. Zhejiang Chinese Medical University.
[19] Zhang, L. (2022). Research on RNA methylation site prediction methods based on deep learning algorithms. Shanghai Maritime University.
[20] Li, F., Yuan, L., Lu, H., et al. (2022). Deep learning-based kcat prediction enables improved enzyme-constrained model reconstruction. Nature Catalysis, 5, 662-672.
[21] Song, Y., Yuan, Q., Chen, S., et al. (2024). Accurately predicting enzyme functions through geometric graph learning on ESMFold-predicted structures. Nature Communications, 15, 8180.
[22] Ramos, A. I., Cordeiro, L. M., & Pinheiro, F. C. (2025). The influence of an AI-driven personalized nutrition program on the human gut microbiome and its health implications. Nutrients, 17(7), 1260.