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Mini-Review Article

Nutrigenomics and Jamu: Integrating Nutritional Genomics with Indonesian Traditional Medicine for Precision, Preventive, and Systems-Oriented Health

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Abstract

Nutrigenomics and nutrigenetics often grouped under nutritional genomics investigate how nutrients and bioactive food compounds modulate gene expression and related molecular phenotypes, and how genetic variation modifies individual responses to diet. These approaches are increasingly operationalized through multi-omics (transcriptomics, epigenomics, metabolomics, proteomics, microbiomics) and data-driven dietary interventions, including randomized controlled trials in personalized nutrition. In parallel, Indonesian jamu an ancestral system of multi-herb preparations used for health maintenance and symptom management represents a rich, under-modeled source of phytochemical diversity and culturally embedded dietary practices. This review synthesizes evidence at the intersection of nutrigenomics and jamu by (1) outlining core concepts and methodological standards in nutritional genomics; (2) summarizing translational frameworks for connecting botanical complexity to molecular mechanisms using systems biology, network pharmacology, and multi-omics; and (3) appraising representative jamu-relevant botanicals (e.g., Curcuma longa, Zingiber officinale, Andrographis paniculata, Centella asiatica) for nutrigenomic effects on inflammatory, antioxidant, metabolic, and mitochondrial pathways. We propose an implementation pathway for "precision jamu nutrition" that aligns cultural acceptability with clinical governance, quality systems, and evidence hierarchies, emphasizing standardized extracts, rigorous phenotyping, genotype-aware subgroup analyses, and safety monitoring. Key challenges include botanical variability, confounding from complex diets, population genetic diversity, limited prospective trials, and regulatory harmonization. Future research should prioritize pragmatic trials embedded in health services, mechanistic sub-studies leveraging omics, and equitable governance to prevent widening health disparities in precision nutrition.

Keywords: nutrigenomics; nutrigenetics; precision nutrition; Indonesian jamu; phytochemicals; multi-omics; gene expression; epigenetics; microbiome; systems pharmacology.

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1. Introduction

Nutritional genomics has matured from a conceptual interface between diet and the genome into a practical translational field that informs precision nutrition, prevention strategies, and mechanistic understanding of diet-related disease. Seminal reviews defined nutrigenomics as the study of how dietary exposures alter gene expression and downstream molecular phenotypes, and nutrigenetics as the study of how inherited genetic variation modifies dietary response and disease risk [1], [2]. These domains now sit within an ecosystem of multi-omics, computational biology, and increasingly pragmatic clinical trials evaluating whether "personalized" dietary advice produces measurable behavior and health outcomes [3], [4].

In many countries, especially in Asia, diet is not only a set of macro- and micronutrient inputs but also a vehicle for medicinal traditions. Indonesia offers an especially relevant case through jamu multi-component preparations made from rhizomes, leaves, barks, seeds, fruits, and occasionally animal/mineral ingredients used for stamina, digestion, women's health, musculoskeletal pain, and a broad set of symptoms that overlap with chronic inflammation, metabolic dysregulation, and age-related decline. A comprehensive scientific review describes how jamu remains widely used and is increasingly being developed toward rational phytopharmacological use and standardized products [5].

Despite the long history and social legitimacy of jamu, its integration into modern evidence frameworks faces recurring barriers: variability of raw materials, unclear dose–response relationships, limited biomarker-driven evaluation, and heterogeneity of formulas across regions and practitioner lineages [6]. Nutrigenomics offers an opportunity to address several of these constraints because it is designed to map "complex exposures" to molecular response patterns precisely what multi-herb formulations and diet-embedded botanicals represent. Moreover, the dominant biological pathways targeted by many jamu botanicals NF-κB inflammation signaling, Nrf2 oxidative stress responses, mitochondrial bioenergetics, metabolic transcription factors (e.g., PPARs), and gut microbiome interactions are central foci of nutritional genomics [7], [8], [9].

This review is organized as follows. First, we establish definitions, conceptual models, and methodological standards for nutrigenomics/nutrigenetics. Second, we describe a pragmatic review method and evidence-synthesis approach. Third, we discuss results across four translational layers: (1) mechanistic nutrigenomics; (2) genotype-dependent response and precision nutrition trials; (3) botanical and dietary phytochemical nutrigenomics; and (4) jamu-specific considerations including standardization, quality, and health system implementation. We conclude with a research and implementation agenda for a "precision jamu nutrition" pipeline that is scientifically rigorous and culturally responsive.

2 Methods

Design and scope. This article is a narrative review with structured elements. The scope includes (a) foundational nutrigenomics and nutrigenetics concepts; (b) clinical and public health translation through personalized nutrition; and (c) mechanistic and systems-level evidence relevant to jamu botanicals that are commonly used as dietary agents or medicinal foods in Indonesia.

Search strategy. We prioritized peer-reviewed articles indexed in PubMed and publisher platforms, focusing on reviews, methodological standards, and representative mechanistic and clinical studies. Search terms included combinations of: "nutrigenomics", "nutrigenetics", "precision nutrition", "personalized nutrition trial", "gene expression", "epigenetics", "microbiome", and

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jamu-relevant botanicals (e.g., "Curcuma longa", "curcumin", "Zingiber officinale", "ginger", "Andrographis paniculata", "andrographolide", "Centella asiatica").

Inclusion criteria. References were included if they (1) are verifiable journal publications; (2) provide a DOI; and (3) materially contribute to at least one review objective (definition, method, mechanistic pathway, translational trial, or jamu/botanical context). Priority was given to higher-quality evidence (systematic reviews, meta-analyses, RCTs, and widely cited mechanistic reviews), while recognizing that mechanistic work is often preclinical and that jamu formulas are heterogeneous.

Synthesis approach. Evidence was synthesized into a translational framework linking exposure (diet/botanicals/formulas) to intermediate molecular phenotypes (gene expression, epigenetic marks, metabolite signatures), to clinical endpoints. We also incorporated a quality-by-design lens for botanicals: identity, purity, dose standardization, chemical profiling, and reproducibility across batches. Limitations and risks of bias are discussed in the Results and Discussion.

3 Results and Discussion

3.1 Nutrigenomics foundations: definitions, causal models, and measurement

Nutrigenomics and nutrigenetics were introduced as post-genomic disciplines to address a persistent empirical gap: the same dietary guidance yields heterogeneous outcomes across individuals. Early work proposed that nutrients and bioactive food chemicals could be treated as environmental signals that modify gene expression and molecular pathways long before disease becomes clinically detectable **[1]**. In this framing, the "diet → gene regulation → phenotype" pathway becomes a measurable causal chain rather than a metaphor.

A practical causal model in nutrigenomics typically includes: (a) exposure (dietary intake, timing, matrix, co-exposures); (b) internal dose (absorption, metabolism, distribution); (c) molecular response (gene expression, epigenetic marks, proteins, metabolites); and (d) clinical phenotype (symptoms, biomarkers, disease incidence). Genetic variation influences multiple nodes: taste and preference affecting exposure; enzymes affecting internal dose; receptor variants affecting signaling; and baseline disease risk altering the slope of response. For botanicals, genetic variation also influences the microbiome-mediated transformation of phytochemicals into bioactive metabolites.

Measurement has progressed from candidate gene assays to integrated multi-omics. Transcriptomics measures gene expression across thousands of genes. Epigenomics captures persistent modifications such as DNA methylation that mediate long-horizon responses. Metabolomics serves as both exposure assessment (nutrient and phytochemical metabolites) and response assessment (lipids, amino acids, inflammatory mediators). Microbiome profiling adds a crucial interface because microbial metabolism can reshape the chemical nature and bioactivity of many dietary compounds. The methodological implication is that high-dimensional data require disciplined analysis plans, including pathway-level hypotheses, appropriate multiple-testing control, and external validation where possible.

3.2 Study designs and evidentiary standards in nutritional genomics

Nutrigenomics research has historically faced inconsistent findings due to small sample sizes, unmeasured confounding, and variable exposure ascertainment. Candidate gene–diet interaction studies are particularly vulnerable because many interactions are modest and can be inflated by publication bias. Consequently, modern best practice emphasizes: (1) adequately powered designs;

(2) prespecified hypotheses; (3) replication; (4) repeated exposure and outcome measures; and (5) careful control of population stratification when genetic information is used.

Randomized controlled trials remain the gold standard for causal inference in nutrition, but they are resource intensive. Personalized nutrition trials provide a useful compromise because they can test feasibility and behavior change at scale while permitting mechanistic sub-studies. The Food4Me randomized trial demonstrated that personalized nutrition advice can produce beneficial behavior changes compared with conventional approaches [3]. Subsequent Food4Me analyses reported improvements in specific dietary components, such as reductions in discretionary foods and beverages [4]. These findings are relevant to jamu because many jamu preparations are consumed as "functional beverages," and a realistic translation pathway is to embed standardized jamu within personalized dietary counseling rather than positioning it as a stand-alone pharmacotherapy.

For botanicals, evidentiary standards add an additional axis: product identity. Inadequate characterization of botanical interventions leads to non-replicable results even if study design is strong. A nutrigenomics-grade botanical trial therefore requires (a) authenticated species identity; (b) standardized extraction and marker compounds; (c) stability and batch tracking; and (d) documented dosing regimen. Without these elements, omics signatures cannot be confidently attributed to the intervention.

3.3 Mechanistic pathway hubs: NF-κB, Nrf2, metabolic transcription factors, and mitochondria

Across nutrigenomics and botanical research, two transcriptional hubs are repeatedly implicated in diet-related inflammation and oxidative stress: NF-κB and Nrf2. NF-κB regulates pro-inflammatory cytokines and enzymes; Nrf2 governs antioxidant and cytoprotective genes. A concise review describes NF-κB and Nrf2 as prime molecular targets for chemoprevention and cytoprotection by dietary phytochemicals, highlighting mechanistic crosstalk between inflammatory and antioxidant programs [7].

Metabolic transcription factors provide a third hub. PPARα/γ, SREBP, and related regulators orchestrate lipid handling, insulin sensitivity, and adipocyte differentiation. Nutrient composition and phytochemicals can modulate these networks, producing measurable metabolomic and transcriptional changes. Finally, mitochondrial function and oxidative phosphorylation represent a fourth hub: dietary patterns and certain botanicals can shift mitochondrial biogenesis, respiration, and redox status, which then influences fatigue, aging phenotypes, and inflammatory tone.

For jamu, these hubs offer a practical mechanism taxonomy. Many jamu botanicals plausibly exert effects by modestly shifting NF-κB activity (reduced inflammatory gene expression) and/or increasing Nrf2 target genes (enhanced antioxidant defense), with secondary effects on metabolic transcription factors and mitochondria. This expectation is testable with transcriptomic panels and pathway scores rather than single biomarkers.

3.4 Jamu as an exposure system: cultural practice, chemical diversity, and translation constraints

A central insight for integrating nutrigenomics with jamu is that jamu is best modeled as an "exposure system" rather than a single agent. Jamu is consumed in many forms (decoctions, powders, capsules, functional drinks), in variable dosing, and often alongside dietary patterns. This resembles how nutrigenomics treats dietary patterns rather than isolated nutrients. A review of jamu emphasizes its cultural embeddedness and the scientific and regulatory work needed to move toward rational phytopharmacological use, including quality and standardization [5].

From a translational perspective, jamu sits at the intersection of three domains: (1) food and culinary practice; (2) traditional medicine; and (3) modern phytopharmaceutical development [10]. Nutrigenomics can contribute most when jamu is positioned in a clearly defined domain for a given project. For example, if jamu is treated as a functional food, endpoints might include metabolic risk factors and diet quality; if treated as supportive traditional medicine, endpoints might include symptom relief and quality of life; if treated as a phytopharmaceutical candidate, endpoints might include disease-specific outcomes, stringent safety monitoring, and tightly controlled dosing.

The primary constraints include botanical variability, limited pharmacokinetic data for many formulations, co-use with modern drugs, and lack of large prospective trials. These constraints are not unique to jamu; they mirror challenges in many botanical systems. However, Indonesia's biodiversity and high prevalence of use make jamu a strategic context where nutrigenomics can generate both mechanistic insight and practical guidance if research infrastructure and governance are aligned.

3.5 Representative jamu botanicals as nutrigenomic modulators: Curcuma longa (turmeric)/curcumin

Curcumin is a canonical example of a dietary phytochemical with broad gene-regulatory effects. Mechanistic reviews document that curcumin modulates transcription factors such as NF-κB, AP-1, and STAT, and regulates genes involved in inflammation, growth signaling, apoptosis, and cell cycle control [11]. In nutrigenomic framing, curcumin functions as a "pleiotropic signal" that can shift multiple networks rather than acting as a single-target drug.

Because turmeric is commonly used in both culinary and medicinal contexts, real-world exposure is frequent but heterogeneous. This creates both opportunity and risk: opportunity to study effects in pragmatic settings, and risk of misclassification if exposure is not quantified. High-quality nutrigenomic studies should therefore include biomarkers of exposure (curcumin metabolites where feasible), record preparation method (fresh, dried, decoction, extract), and account for fat co-ingestion that affects absorption.

A practical study architecture is to combine standardized curcumin or turmeric preparations with short-term transcriptomic readouts (e.g., PBMC gene expression panels for NF-κB and Nrf2 target genes), then follow with longer-term endpoints such as inflammatory markers and metabolic risk factors. Multi-omics can help distinguish responders from non-responders: some individuals may show clear reductions in inflammatory transcriptional signatures while others show minimal molecular response, plausibly due to microbiome and metabolism differences.

Curcumin's gene-regulatory effects can also be evaluated using integrative transcriptome–metabolome studies in model organisms. For example, transcriptomic studies have shown that curcumin can induce large but dynamic shifts in gene expression programs, illustrating the importance of timing and dose in interpreting nutrigenomic responses [12]. Although such models are not direct evidence for clinical benefit, they provide methodological lessons about transient vs. sustained gene expression changes.

3.6 Representative jamu botanicals as nutrigenomic modulators: Zingiber officinale (ginger)/gingerols and shogaols

Ginger-derived phenolics have been reviewed for chemopreventive and anti-inflammatory actions, including mechanisms that involve altered gene expression, antioxidant pathways, and apoptosis induction [13]. In nutrigenomic framing, ginger can be conceptualized as a modulator of stress-response and inflammatory transcriptional states, potentially shifting gene expression in immune and epithelial cells.

For jamu and Indonesian dietary practice, ginger is frequently consumed as a beverage ingredient and rhizome component in formulations targeting digestive comfort, nausea, and general vitality. This overlap between food and medicine suggests that ginger studies should explicitly model dietary background and habitual intake. Acute challenge designs (e.g., standardized ginger beverage plus high-fat meal) can test whether ginger modifies postprandial inflammatory gene expression patterns, a pathway relevant to metabolic inflammation.

Translationally, the goal is to move from broad claims ("anti-inflammatory") to measurable signatures. For instance, a pathway score capturing Nrf2 target gene induction, or NF-κB target gene suppression can be prespecified and tested in early-phase trials. This approach reduces multiple-testing problems and produces interpretable outputs for product development and dietary counseling.

3.7 Representative jamu botanicals as nutrigenomic modulators: Andrographis paniculata (sambiloto)/andrographolide

Andrographolide and related diterpenoids from Andrographis paniculata are widely studied for anti-inflammatory actions. Experimental and translational work indicates suppression of NF-κB activation and downstream pro-inflammatory gene programs in relevant models [14]. Such pathway-level suppression fits directly into a nutrigenomic signature focused on reduced inflammatory transcriptional activity.

Mechanistic specificity is important because "anti-inflammatory" is not a unitary phenotype. NF-κB suppression can occur at multiple nodes (IKK activation, IκB degradation, nuclear translocation, DNA binding), and different botanicals may act at different nodes. For example, andrographolide has been reported to inhibit NF-κB activation through signaling cascades in vascular smooth muscle cell models [15], reinforcing the plausibility of transcription-level effects.

From a translational standpoint, sambiloto's bitter taste and potential gastrointestinal side effects can affect adherence, making dose-finding and tolerability assessment essential. Precision jamu nutrition would incorporate phenotype selection (e.g., individuals with elevated inflammatory markers or specific symptom patterns) and then test whether gene expression signatures shift as expected. Safety and governance remain central: standardized marker-based extracts and contaminant screening are prerequisites for credible nutrigenomic inference.

Evidence also supports exploration of modified andrographolide derivatives (e.g., sulfonate forms) in inflammatory models, including suppression of NF-κB activation in viral-mimetic lung inflammation contexts [16]. While such studies sit closer to pharmacology than nutrition, they provide mechanistic anchors that can inform nutrigenomic hypotheses for dietary-grade preparations.

3.8 Representative jamu botanicals as nutrigenomic modulators: Centella asiatica (pegagan) / triterpenoids and mitochondrial programs

Centella asiatica provides a compelling case for integrating plant omics (to understand biosynthetic pathways and quality control) with host-response omics (to understand molecular effects). Transcriptome assembly and gene mapping studies in Centella identify candidate genes involved in secondary metabolism, supporting a mechanistic basis for standardization and cultivation strategies [17]. More recent integrated metabolome–transcriptome analyses refine candidate genes for triterpenoid saponin biosynthesis [18].

From the host-response side, experimental evidence suggests that Centella can promote antioxidant gene expression and mitochondrial oxidative respiration in inflammatory neuroimmune models, highlighting nutrigenomic signatures relevant to neuroprotection and fatigue-related phenotypes [19]. This aligns with traditional uses of pegagan in cognition and revitalization.

For precision jamu nutrition, pegagan illustrates a two-track standardization strategy: (1) upstream plant biology to control metabolite profiles (genotype selection, cultivation conditions), and (2) downstream product standardization via marker compounds and untargeted metabolomic fingerprints. This two-track strategy is particularly valuable when clinical hypotheses depend on specific metabolite classes (e.g., triterpenoid saponins) whose concentrations vary widely by cultivation and processing.

3.9 Systems biology approaches for multi-herb formulations

A defining feature of jamu is combinatorial complexity: multi-herb formulas may contain dozens of metabolites with overlapping and sometimes opposing biological effects. Nutrigenomics faces an analogous challenge when interpreting whole diets, dietary patterns, and food matrices. Systems biology provides a bridge by enabling pathway and network analyses rather than single-target claims.

A systems jamu nutrigenomics workflow can be structured as: (1) chemical characterization of the formulation (targeted markers + untargeted metabolomics); (2) prediction and mapping of bioactivity networks (known targets, transcription factor perturbations, pathway enrichment); (3) preclinical verification using relevant models with transcriptomic profiling; (4) early-phase human studies to detect molecular signatures in accessible tissues (blood, stool, urine) and to evaluate safety; and (5) pragmatic trials embedding jamu in dietary advice or health service pathways with standardized products.

Network-level interpretation is crucial because many phytochemicals act as weak ligands or modulators that cumulatively shift regulatory states. For example, concurrent mild activation of Nrf2 and inhibition of NF-κB can produce a coherent anti-inflammatory/antioxidant signature without any single compound being dominant. Conversely, mixtures can create antagonism or toxicity if doses are uncontrolled. Therefore, nutrigenomic studies of jamu must integrate exposure quantification, bioavailability considerations, and safety profiling as first-class variables.

3.10 Epigenetics, microbiome, and long-horizon effects

A major promise of nutrigenomics is explaining how dietary exposures can produce durable biological changes through epigenetic mechanisms and microbiome-mediated pathways. Epigenetic marks (e.g., DNA methylation) can integrate cumulative exposures and may mediate long-term risk modulation for cardiometabolic disease and inflammation. While many phytochemicals have been proposed as epigenetic modulators, actionability for clinical counseling remains limited without prospective evidence and clear dose–response characterization.

The gut microbiome adds an additional layer especially relevant to jamu, because many jamu botanicals are rich in fibers and polyphenols that can be transformed into metabolites with distinct bioactivities. Microbiome composition can thus function as both an exposure modifier (determining metabolite production) and an outcome mediator (shifting immune and metabolic regulation). Precision jamu nutrition should therefore consider stool-based profiling and metabolomics where feasible, or at minimum, measure microbial-derived metabolites that act as functional readouts.

From a study design perspective, the most informative approach is longitudinal sampling with repeated measures: baseline, early response (days to weeks), and sustained response (months). This separation is crucial because transcriptional shifts can be rapid and transient, while microbiome and epigenetic changes may require longer exposure. Tiered sampling (full omics in a sub-cohort) can maintain feasibility while preserving mechanistic insight.

3.11 Governance: quality systems, safety, ethics, and regulatory alignment

Any attempt to connect jamu to nutrigenomics must confront a practical constraint: if exposure is not well-characterized, molecular inference can be misleading. Botanical variability arises from species identity errors, cultivation conditions, harvest timing, post-harvest processing, and storage. Moreover, informal markets can introduce contamination (microbial, heavy metals) or adulteration. Precision jamu nutrition therefore requires quality systems analogous to those used in modern phytopharmaceutical development: authenticated raw materials, standardized extraction methods, marker-based specification, stability testing, and batch traceability.

Safety governance is equally essential. Nutrigenomic readouts are not substitutes for clinical safety monitoring; omics can create false reassurance if not anchored to adverse event tracking and clinical chemistry. A minimum safety package should include hepatic and renal monitoring in early-phase studies, plus interaction screening with common pharmaceuticals. This is particularly relevant because jamu is often used by individuals with chronic disease who may co-use modern drugs.

Ethically, precision nutrition introduces concerns about equity and interpretation. Genotype data can be misused or overclaimed. Reviews of nutrigenomics emphasize careful translation, transparent communication of uncertainty, and avoidance of deterministic claims. A staged approach phenotype-first personalization, then genotype where actionability is proven reduces risk while still capturing precision benefits.

3.12 Proposed research agenda and implementation framework for "precision jamu nutrition"

Data integration and reproducibility. High-dimensional omics introduce reproducibility risks unless analytical pipelines are standardized. Preprocessing choices (normalization methods, batch correction, feature selection) can materially affect results. Therefore, precision jamu nutrigenomics should adopt transparent, version-controlled pipelines and preregistered analysis plans. Where feasible, de-identified datasets and code should be shared to enable secondary analysis and replication. This is not only a scientific issue; it directly impacts public trust in traditional medicine modernization efforts.

Biostatistical considerations in heterogeneous populations. Indonesia's population diversity and regional dietary differences imply that nutrigenomic signals may differ across subpopulations. Analyses should therefore test for effect modification by ancestry proxies, region, and diet pattern.

Mixed-effects models can include site or region as random effects, and sensitivity analyses can evaluate robustness to population stratification. Importantly, heterogeneity should not be treated only as noise; it can indicate meaningful gene–environment structure that supports personalized guidance.

Intervention adherence and behavior change. Nutrigenomic interventions fail if adherence is poor. Jamu formulations that are bitter or time-consuming to prepare may reduce adherence, and nutrigenomic readouts can then reflect nonadherence rather than nonresponse. Behavioral strategies simplified dosing, culturally acceptable delivery formats, and feedback are therefore crucial. Personalized nutrition trials demonstrate that tailored feedback can improve dietary behavior [3]. Jamu studies can adapt these lessons by providing culturally resonant counseling and simple tracking tools.

Safety signal detection with omics. Omics can also support safety monitoring. For example, unexpected elevations in stress-response gene programs or metabolomic markers of hepatic strain could prompt closer clinical assessment. However, such signals must be interpreted cautiously and validated. The best use of omics for safety is hypothesis-driven and integrated with clinical labs rather than treated as an exploratory safety net. In early phase jamu trials, combining standard clinical chemistry with targeted transcriptomic panels may help identify early warning patterns.

Regulatory science and claim substantiation. Different product categories imply different allowable claims. Precision jamu nutrition research should explicitly map outcomes to allowable claims under the intended category. If the product is positioned as a functional food, claims should be limited and supported by nutrition-style evidence. If positioned as a traditional medicine product, claims may focus on supportive indications with traditional plausibility. Escalating to phytopharmaceutical claims requires higher-level evidence and stricter quality standards. Aligning research endpoints to regulatory pathways prevents wasted effort and accelerates translation.

Ethics of genetic testing and informed consent. Where genetic data are collected, informed consent must cover potential secondary uses, data governance, and privacy. Participants should understand that genetic results may have uncertain implications and should not be used to make medical decisions without professional guidance. In service settings, genetic testing should be offered only when actionable and equitably accessible; otherwise, it risks widening disparities and undermining trust in both nutrigenomics and jamu modernization.

Linking plant omics to human response: a continuity model. Plant transcriptomics and metabolomics can be used to engineer consistency in active metabolite profiles, which in turn improves interpretability of human nutrigenomic response. For pegagan, plant transcriptome mapping and metabolome–transcriptome integration support identification of genes underlying triterpenoid biosynthesis [17], [18]. Similar approaches can be applied to other jamu botanicals to stabilize phytochemical composition across cultivation sites. This creates continuity from farm to clinic, which is a prerequisite for credible precision claims.

Real-world evidence and pragmatic trial embedding. Because jamu is already widely used, real-world evidence can complement RCTs. Pragmatic trials embedded in routine care can compare standardized jamu plus counseling versus counseling alone, while collecting a minimal biomarker set and optional omics. The aim is to generate policy-relevant evidence under realistic conditions. Such designs are particularly suitable for Indonesia, where cultural uptake is high but controlled clinical trial resources may be limited.

Case example: metabolic inflammation phenotype. A concrete near-term target for precision jamu nutrition is metabolic inflammation. Individuals with insulin resistance and elevated

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inflammatory markers may be more likely to exhibit measurable NF-κB and Nrf2 pathway changes in response to certain botanicals. A standardized turmeric–ginger formulation could be tested for its impact on postprandial inflammation and lipid metabolites, with transcriptomic pathway scores as intermediate endpoints. The hypothesis is that molecular response predicts improvements in diet quality and metabolic markers over time.

Case example: fatigue and mitochondrial phenotype. A second target is fatigue-related phenotypes potentially linked to mitochondrial function and oxidative stress. Pegagan-containing formulations could be studied using mitochondrial gene expression scores and oxidative stress metabolomics, alongside validated fatigue, and function scales. The objective would not be to overclaim treatment of complex syndromes, but to identify whether a reproducible mitochondrial/antioxidant signature corresponds to improved patient-reported outcomes in a defined population.

A coherent research agenda should progress from feasibility to actionability. Phase 0 should map real-world jamu use patterns (formulas, doses, frequency, co-use with drugs) and identify priority clinical domains (e.g., metabolic syndrome, musculoskeletal pain, fatigue, digestive symptoms). Phase 1 should develop standardized, chemically profiled formulations aligned to those domains, with predefined marker compounds and batch specifications. Phase 2 should run short-term mechanistic studies in humans to detect nutrigenomic signatures typically transcriptomic panels in peripheral blood, targeted cytokines, oxidative stress markers, and metabolomics—while confirming safety. Phase 3 should embed these formulations within pragmatic randomized trials, ideally with behaviorally informed dietary counseling, to test whether molecular signatures translate to meaningful symptom or risk reductions.

Implementation in Indonesian health services requires careful design choices. First, avoid overclaiming genetic personalization before evidence is sufficient; focus initially on phenotype-driven personalization (e.g., insulin resistance phenotype, inflammatory phenotype). Second, build minimal but robust data infrastructure: standardized intake forms, adverse event reporting, and a small set of validated biomarkers, with optional omics in sub-cohorts. Third, ensure cultural acceptability and co-design: jamu's legitimacy depends on community trust and practitioner knowledge, and research designs should respect local frameworks while applying modern methodological rigor. Fourth, prioritize equity: precision nutrition can widen disparities if only affluent groups can access testing and standardized products.

From a nutrigenomic analytics standpoint, multilevel models are preferred because they can incorporate repeated measures and accommodate heterogeneity. Rather than seeking a single universal "signature," studies should prespecify pathway-level hypotheses (e.g., reduced NF-κB transcriptional activity; increased Nrf2 target genes; improved mitochondrial respiration markers) and quantify these as composite scores. Genotype can be integrated as an effect modifier where justified, and microbiome features can be incorporated as mediators or moderators. This approach reduces false discovery and aligns results to biological plausibility.

To operationalize pathway scores, investigators can use curated gene sets (e.g., Nrf2 target genes, NF-κB response genes) and compute standardized enrichment scores for each participant at each time point. These scores can then be linked to metabolomic indicators of exposure and response, such as oxidative stress metabolites or lipid profiles. When feasible, integrating transcriptomics with targeted proteomics provides stronger mechanistic triangulation because protein levels and activity

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often lag transcription. In resource-constrained contexts, a pragmatic compromise is to use targeted qPCR panels for a small number of genes representing each pathway hub.

Product development should proceed in parallel with mechanistic research. A standardized jamu product intended for nutrigenomic study should have (1) a clear botanical identity list with voucher specimens; (2) a chemical specification defining marker compound ranges; (3) stability data supporting shelf life; (4) contaminant and adulterant testing; and (5) a manufacturing process with reproducible yields. Without these elements, any observed molecular signature may be irreproducible. Conversely, robust product specification enables iterative improvement: if a formulation shows a desired pathway signature but inconsistent magnitude, cultivation and processing variables can be adjusted to stabilize metabolite profiles.

Clinical endpoints should be selected to align with mechanisms and practical relevance. For anti-inflammatory signatures, endpoints could include validated symptom scales (e.g., pain, fatigue), inflammatory markers, and functional outcomes. For metabolic signatures, endpoints include fasting glucose, insulin resistance indices, triglycerides, and postprandial responses. For mitochondrial/oxidative signatures, endpoints could include exercise tolerance proxies or fatigue scales, though these require careful trial design to avoid placebo-driven artifacts. Importantly, endpoints must be feasible in Indonesian service contexts and interpretable by clinicians and policymakers.

A useful concept is "signature-to-service translation." If a formulation repeatedly produces a reproducible molecular signature (e.g., reduced NF-κB gene expression score) and this signature is associated with improved patient-relevant outcomes, then the signature can become a quality-linked biomarker used during scale-up. This is analogous to how some pharmacodynamic biomarkers are used in drug development. In nutrigenomics, the bar for biomarker adoption must be high because dietary exposures are variable; nonetheless, the concept provides a route to evidence-based standardization rather than relying solely on historical use.

Finally, communication strategies must be carefully managed. Precision jamu nutrition should be framed as "evidence-informed personalization" rather than genetic determinism. Patients should be informed that genetic factors can modify response but do not guarantee outcomes, and that lifestyle context remains central. Regulatory communication should avoid disease treatment claims unless supported by high-grade evidence and appropriate product classification. A credible pathway is to focus on supportive and preventive claims linked to biomarkers, then escalate claims only if large trials substantiate them.

3.13 Nutrigenetics: gene–diet interactions and what is realistically actionable

Nutrigenetics asks a practical question: does inherited variation meaningfully change what dietary advice should be given to an individual? Foundational work positioned nutrigenetics as an extension of gene–environment interaction research, with clear actionability in rare monogenic contexts (e.g., phenylketonuria) and more complex, probabilistic implications in common multifactorial disease [2]. In complex disease, gene–diet interactions often have modest effect sizes and can be context-dependent, which makes uncritical translation to consumer recommendations risky.

In a precision jamu nutrition context, the relevant question is not "Which jamu for which gene?" but "Which biological constraints shape exposure and response?" Potential constraints include variants influencing inflammation and oxidative stress pathways, phase I/II metabolism, and transporters affecting internal dose. While the review literature supports the plausibility of such modifiers, clinical actionability requires replicated evidence showing that a genotype-informed choice produces better outcomes than phenotype-only choices. Until such evidence exists, genotype should be used primarily for research stratification and hypothesis generation.

A pragmatic intermediate step is to use genotype to interpret heterogeneity rather than dictate choices. For example, if a standardized curcumin formulation produces a strong anti-inflammatory transcriptional signature in a subset of participants, genetic differences in inflammatory signaling or metabolism can be explored as explanatory variables. This approach strengthens mechanistic understanding while avoiding premature personalized claims.

3.14 Precision nutrition analytics: from biomarkers to algorithms

Precision nutrition increasingly uses algorithmic models to predict glycemic responses, weight change, or inflammatory biomarker changes from baseline data. The methodological core is featuring integration: dietary intake measures, clinical labs, anthropometrics, activity, sleep, microbiome features, and, in some cases, genetic variants. For jamu, analogous models could predict who is likely to exhibit a desirable pathway signature in response to a standardized formulation, using baseline phenotype and dietary context as predictors.

Model development must prioritize external validation and clinical interpretability. High accuracy in one cohort may not generalize across regions with different diets, genetic backgrounds, and product compositions. Therefore, Indonesian deployment should emphasize model transportability: use nested validation, multi-site cohorts, and calibration analyses. Where models are used, they should support clinician and patient decision-making rather than replace it—particularly because botanical products have variable evidence quality and safety profiles.

A practical implementation is to develop "decision support layers" rather than black-box recommendations. For instance, a model might produce a probability of response to a ginger–turmeric formulation, but the output should be accompanied by (a) the expected molecular signature, (b) the expected symptom/risk-factor change, (c) safety considerations, and (d) the level of evidence. This aligns precision nutrition with evidence-based practice and reduces misuse.

3.15 Exposure assessment in jamu nutrigenomics: the central measurement problem

The dominant technical limitation in nutrition research is exposure assessment. Self-reported dietary intake is imperfect; for jamu, exposure variability can be even larger because formulas vary, preparations differ, and consumers may not know exact ingredients or doses. Nutrigenomics can partially mitigate exposure uncertainty by using metabolomics as an objective exposure readout, but only when relevant metabolites are measurable and specific to the botanical.

Therefore, precision jamu nutrition studies should implement a layered exposure strategy. Layer 1 is product specification: participants receive a standardized preparation with defined dosing. Layer 2 is adherence tracking, ideally with simple logs and periodic counts of returned sachets/capsules. Layer 3 is chemical exposure validation, such as targeted metabolite panels (when feasible) or untargeted metabolomic fingerprints that can identify whether exposure patterns match expected profiles. Layer 4 is contextual diet assessment, because background diet can modulate both exposure and response.

This layered approach is resource intensive, but it is the only defensible route for interpreting gene expression signatures. Without exposure fidelity, "non-response" may simply indicate underexposure or substitution with nonstandard products. Conversely, consistent exposure measurement enables learning: investigators can map dose–signature relationships and optimize dosing for tolerability and efficacy.

3.16 Standardization and phytochemical complexity: why marker compounds are necessary but insufficient

Botanical standardization often uses one or two marker compounds (e.g., curcumin content in turmeric extracts) to set specifications. Marker compounds are necessary for identity and batch control, but they are insufficient to capture the full bioactivity profile of multi-component botanicals. Two batches with identical marker levels may differ substantially in minor constituents that influence absorption, metabolism, or pathway modulation.

A nutrigenomics-aligned standardization strategy therefore combines marker compounds with global fingerprints typically untargeted LC-MS metabolomic profiles plus bioactivity-linked assays. For example, a formulation can be characterized by its ability to modulate NF-κB reporter activity or induce Nrf2 target genes in a standardized in vitro assay. While such assays are not clinical endpoints, they function as quality-linked surrogates during manufacturing and scale-up.

Centella exemplifies this logic: plant transcriptomics and metabolomics can explain why triterpenoid profiles differ across cultivation conditions [17], [18]. Translationally, such plant-level data can be used to select cultivation systems that yield more consistent metabolite signatures, which then improves reproducibility of human nutrigenomic responses.

3.17 Safety, drug–herb interactions, and the limits of "natural" assumptions

A recurring public misconception is that "natural" implies safe. Botanical products can produce adverse effects through intrinsic toxicity, contaminants, adulterants, or interactions with pharmaceuticals. Precision jamu nutrition therefore requires a safety-first posture: standardized products, contaminant testing, and proactive interaction screening for common drugs (e.g., anticoagulants, antidiabetics).

Mechanistically, many phytochemicals modulate enzyme and transporter systems that influence drug metabolism. While this review focuses on nutrigenomic signatures rather than pharmacokinetics, the two are connected: altered expression of detoxification genes or inflammatory pathways can influence metabolism and vice versa. Therefore, early-phase trials should monitor clinical labs and adverse events and should exclude high-risk populations unless strong safety data exist.

Omics can support safety only as an adjunct. Unexpected activation of stress-response gene sets or metabolomic patterns suggestive of hepatic strain should trigger clinical follow-up, but omics alone should not be used to declare safety. This is especially important for health system integration, where governance standards must meet clinical expectations.

3.18 Equity and implementation: preventing precision nutrition from widening disparities

Precision nutrition and nutrigenomics often require testing and data infrastructure that can be expensive. If precision jamu nutrition becomes accessible only to high-income groups, it could widen disparities and undermine public trust. Equity must therefore be designed into the implementation model from the beginning.

One equity strategy is tiered precision. Tier 1 uses low-cost phenotyping (BMI, blood pressure, fasting glucose, lipid profile) and standardized products with conservative claims. Tier 2 adds

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targeted biomarkers (inflammatory markers, oxidative stress proxies). Tier 3 includes omics and genotype for research and complex cases. This tiering allows broad access while still enabling advanced research where appropriate.

Cultural equity is also important. Jamu knowledge is often community-based; modernization efforts should be co-designed with practitioners and communities to avoid extractive dynamics. Evidence-based standardization should be framed as strengthening trust and safety rather than replacing tradition with external authority.

3.19 Case pathway: from culinary jamu to clinically governed functional beverages

A realistic translation pathway is to focus on jamu consumed as beverages and culinary additives—formats already integrated into daily life. Functional beverage interventions can leverage personalized nutrition counseling structures and can be deployed in workplaces, primary care settings, or community health programs. Because beverages are easier to dose and standardize than individualized decoctions, they provide a practical entry point for nutrigenomic evaluation.

For example, a standardized ginger–turmeric beverage can be formulated with defined marker content and stability testing, then evaluated for its impact on postprandial inflammatory gene expression scores, oxidative stress markers, and self-reported digestive comfort. The primary goal would be to establish feasibility, adherence, safety, and molecular signal detection. Only after reproducible signatures are shown should larger, longer trials test metabolic endpoints.

This pathway aligns with evidence hierarchies: start with proximal mechanistic outcomes, then progress to distal clinical outcomes. It also aligns with regulatory reality: beverage-based products are more naturally positioned within food/supplement categories, where claims must be conservative and evidence requirements are distinct from drugs.

3.20 Interpreting molecular signatures: avoiding overfitting and false certainty

Omics datasets can generate compelling heatmaps and pathway charts, but interpretation can drift into overclaiming if not disciplined. The most common pitfalls include multiple testing without correction, selective reporting of pathways that "look good," and conflating association with causation. Precision jamu nutrition must adopt practices that reduce these risks: prespecified signatures, correction for multiple comparisons, and validation cohorts.

Interpretation should also distinguish between "directional plausibility" and "clinical meaning." A reduction in NF-κB target gene expression can be biologically plausible, but its clinical meaning depends on magnitude, persistence, and whether it correlates with improved outcomes. Therefore, studies should report effect sizes and link signatures to endpoints rather than presenting signatures as endpoints in themselves.

A pragmatic approach is to define a small number of signatures aligned to the four hub domains (inflammation, antioxidant defense, metabolism, mitochondria) and treat them as intermediate biomarkers. This creates consistency across studies and allows meta-analytic synthesis, accelerating evidence accumulation.

3.21 Botanical–microbiome interactions: a precision lever for jamu

Many phytochemicals are transformed by gut microbes into metabolites with distinct bioactivity. This implies that the microbiome can act as a precision lever: individuals with different microbial configurations may experience different internal doses and different nutrigenomic responses. In practice, this helps explain why the same botanical intervention can yield variable outcomes.

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For jamu, a key hypothesis is that habitual dietary patterns—fiber intake, fermented foods, spice consumption shape the microbiome in ways that influence botanical response. Therefore, precision jamu nutrition studies should measure baseline dietary pattern and microbiome features, then test whether they moderate pathway signatures. Where stool sequencing is not feasible, targeted metabolomics of microbial-derived metabolites can provide functional proxies.

If microbiome moderation is confirmed, translation could include dietary co-interventions that optimize botanical metabolism (e.g., increased prebiotic fiber) or dosing strategies tuned to microbiome response profiles. Such approaches must be tested carefully to avoid "stacking complexity" beyond what can be implemented in real settings.

3.22 Positioning jamu within preventive health and systems medicine

A strategic positioning for precision jamu nutrition is preventive and supportive care, where modest pathway shifts can be meaningful over time. Chronic low-grade inflammation and oxidative stress contribute to cardiometabolic risk and aging phenotypes. If standardized jamu formulations reliably shift inflammatory and antioxidant signatures, they could complement lifestyle interventions rather than compete with pharmacotherapy.

Systems medicine emphasizes the integration of multiple small interventions diet, activity, sleep, stress management—to shift network states. Jamu, when standardized and safely implemented, can be one node in this network. Nutrigenomics contributes by providing measurable intermediate phenotypes (signatures) that show whether the intervention is doing what it is hypothesized to do, facilitating iterative optimization.

Critically, preventive positioning avoids the ethical and regulatory hazards of claiming cure. It also aligns with cultural practice, where jamu is often used for maintaining balance and vitality. Precision approaches can respect this framing while providing evidence-based guardrails.

3.23 Practical omics toolbox for Indonesian settings

Implementing nutrigenomics does not require full-scale, high-cost omics in every study. A practical "omics toolbox" can be tiered to match resources. Tier A uses targeted biomarkers and small transcript panels: qPCR assays for a curated set of genes representing NF-κB response, Nrf2 targets, and metabolic regulators. Tier B adds targeted metabolomics (e.g., lipid panels, oxidative stress metabolites) and inflammatory protein panels. Tier C adds untargeted metabolomics and RNA-seq in a mechanistic sub-cohort.

For Indonesian institutions, this tiering enables immediate research progress while building capacity for more comprehensive multi-omics. Importantly, tiered designs should be preplanned so that Tier A outputs map onto Tier C outputs; for example, pathway scores derived from qPCR panels should correspond to pathway enrichment results from RNA-seq in the sub-cohort. This mapping allows scalable interpretation and reduces reliance on exploratory analyses.

Data governance must be planned from the start. Even modest molecular datasets can contain sensitive information. Standard operating procedures should cover de-identification, access control, storage, and sharing. For multi-site studies, harmonized protocols are essential to reduce batch effects that can masquerade as nutrigenomic signals.

3.24 Knowledge translation: from manuscripts to guidelines and product labels

For nutrigenomic findings to affect health, they must be translated into actionable guidance. In the jamu context, two translation channels are dominant: clinical counseling (in clinics, wellness

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services, or community programs) and product labeling/communication. Both channels require disciplined claim language. A molecular signature can be communicated as "supports antioxidant defenses" or "supports healthy inflammatory balance" only if evidence demonstrates reproducible biomarker changes and acceptable safety.

Guidelines should specify target populations, dosing regimen, contraindications, and expected time course. They should also emphasize that jamu is complementary to diet and lifestyle, not a replacement. Product labels should disclose standardized marker levels and quality testing to support consumer trust. Where evidence is preliminary, labels should avoid implying disease prevention or treatment.

An important opportunity is to develop clinical decision aids that integrate phenotype markers (e.g., glucose, lipids) with intervention options (diet pattern changes, standardized jamu products) and monitoring plans. In this way, nutrigenomics becomes an accountability system: if expected biomarker shifts do not occur, the intervention is reconsidered rather than continued indefinitely.

3.25 Research prioritization: selecting high-impact jamu candidates for nutrigenomic evaluation

Indonesia's botanical diversity is vast, and a major risk is dispersing research efforts across too many candidates without achieving decisive evidence for any. A prioritization framework can allocate resources to candidates with (1) high prevalence of use, (2) plausible mechanistic alignment with nutrigenomic hubs, (3) feasibility of standardization, and (4) safety plausibility. Turmeric, ginger, sambiloto, and pegagan score well on these criteria and therefore are suitable initial anchors.

Prioritization should also consider "formula archetypes," such as anti-inflammatory tonics, metabolic support formulations, and cognitive/vitality formulations. Studying archetypes rather than idiosyncratic formulas accelerates generalizable learning. For each archetype, a minimal set of pathway signatures and endpoints can be standardized across trials, enabling aggregation of evidence.

Where novel botanicals are considered, early-stage work should focus on chemical characterization and in vitro pathway assays (NF-κB/Nrf2 reporters) before moving to omics-heavy human studies. This pipeline reduces cost and increases the chance that human studies detect meaningful signals.

3.26 Limitations of current evidence and how to address them

This review highlights a clear intersection between nutrigenomics and jamu at the level of mechanistic plausibility and translational opportunity. Nevertheless, several limitations constrain confidence in clinical claims. First, much botanical nutrigenomic evidence is preclinical; translating preclinical pathway modulation to human outcomes is not guaranteed. Second, human studies often use nonstandardized products, complicating reproducibility. Third, nutrigenomic signals can be transient and context-dependent, requiring careful timing of sampling and standardized diet control.

Fourth, publication bias can inflate positive mechanistic narratives. Negative or null results are less likely to be published, making it difficult to estimate true effect sizes. Fifth, Indonesian population diversity and dietary variation require multi-site research for generalizability. These limitations are addressable through pragmatic but rigorous methods: standardized products, prespecified signatures, replication cohorts, and transparent reporting of null findings.

Finally, the ethical dimension must be emphasized. Precision approaches can be misused to market unproven genetic tests or overstated products. A governance framework—combining scientific standards, regulatory alignment, and professional ethics—is necessary to ensure that nutrigenomics strengthens, rather than undermines, the credibility of jamu modernization.

3.27 Future directions: integrating nutrigenomics with digital health and real-time monitoring

Digital health tools can support precision jamu nutrition by improving exposure tracking, adherence, and outcome monitoring. Mobile apps can capture daily intake, symptom scores, and simple lifestyle measures (sleep, activity). Wearables can provide objective proxies for stress and activity that influence inflammatory tone. These data streams can be integrated with periodic biomarker assessments to create individualized feedback loops.

The key is to avoid data overload. A minimalist strategy is often best: a small set of high-value metrics collected consistently. Digital tools should be designed for Indonesian contexts with language, literacy, and connectivity considerations. In research, digital adherence metrics can reduce uncertainty and improve the interpretability of nutrigenomic signatures.

As evidence accumulates, digital decision support can be refined to suggest when to continue, adjust, or discontinue a jamu intervention based on biomarker trajectories and tolerability. This turns nutrigenomics from a static "test" into a dynamic monitoring system, which is more aligned with how lifestyle interventions operate.

3.28 Synthesis: what makes nutrigenomics uniquely valuable for jamu modernization

Traditional botanical research often oscillates between two extremes: isolating single "active compounds" (which can miss synergy and cultural reality) and describing broad traditional use without mechanistic anchoring. Nutrigenomics offers a middle path: it can accommodate complex mixtures and patterns while still delivering measurable, reproducible molecular outputs.

For jamu modernization, this is uniquely valuable. Jamu formulas and culinary practices can be evaluated as complex exposures, producing transcriptional and metabolomic signatures that capture systems-level changes. These signatures can support evidence-based standardization, guide dose optimization, and identify subgroups most likely to benefit. Importantly, nutrigenomic outputs can also reveal when a formulation is biologically inactive at real-world doses, preventing wasted effort and misleading claims.

The practical implication is that nutrigenomics should be integrated early in the jamu research pipeline, not added as an afterthought. When coupled with strong quality systems and pragmatic clinical trials, nutrigenomics can accelerate the development of safe, credible, culturally resonant jamu-based interventions for preventive and supportive health.

3.29 Suggested minimal reporting checklist for precision jamu nutrigenomics studies

To improve comparability and reduce research waste, studies should report a minimal checklist. Product reporting should include botanical species names (with authority), plant parts, extraction method, solvent, marker compounds with ranges, batch numbers, storage conditions, and stability testing. Chemical profiling should include at least one untargeted fingerprint method or an explanation for why it is not feasible.

Participant reporting should include baseline diet assessment method, key phenotypes (BMI, blood pressure, glucose/lipids), medication use, and adverse event monitoring plan. If genetic data are collected, population stratification handling and consent governance should be stated. Outcome reporting should clearly distinguish primary endpoints (clinical or biomarker) from exploratory omics outputs and should include effect sizes with uncertainty intervals.

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Omics reporting should include platform details, preprocessing, normalization, batch correction, and multiple-testing control. Where pathway scores are used, gene sets and scoring method should be specified. Finally, transparency reporting should include preregistration (when applicable), data availability, and code availability. This checklist is modest but would materially improve the credibility of the field.

3.30 Integrating nutrigenomics with the broader Indonesian food system and biodiversity economy

Beyond clinical research, precision jamu nutrition intersects with agriculture, small-scale producers, and biodiversity governance. Standardization requires reliable supply chains, which in turn require cultivation practices that stabilize metabolite profiles. Plant omics and metabolomics can inform cultivation decisions, while quality systems can be adapted for SMEs through cooperative models and shared testing facilities.

A biodiversity economy perspective emphasizes that value capture should benefit local communities and producers. If nutrigenomics increases demand for standardized botanicals, there is risk of overharvesting and ecological pressure. Therefore, sustainable cultivation, fair sourcing, and transparent benefit sharing should be integrated into the research-to-market pathway. This is not ancillary; it affects long-term feasibility and ethics.

Linking nutrigenomic signatures to quality-linked markers can also help producers. If a producer can demonstrate that their product meets a metabolomic fingerprint associated with desired pathway signatures, this creates a premium market based on evidence rather than hype. Such models can align economic incentives with scientific rigor.

3.31 Final recommendations for a 3-year program of work

A pragmatic three-year program can deliver meaningful progress. Year 1 should focus on candidate selection, standardization, and feasibility studies. Deliverables include standardized formulations, analytical methods (marker assays and fingerprints), and pilot mechanistic studies demonstrating detectable pathway signatures. Year 2 should conduct early-phase randomized studies with prespecified signature endpoints, safety monitoring, and iterative optimization of dosing and formulation. Year 3 should execute at least one pragmatic trial embedded in a real service setting, with primary clinical endpoints and a mechanistic sub-cohort for omics.

Throughout the program, governance and ethics should be institutionalized: data management plans, adverse event reporting, and regulatory alignment. Collaboration between universities, hospitals, BPOM-aligned quality labs, and community stakeholders is essential. The program should also include capacity building in omics analysis and phytochemical standardization, ensuring sustainability beyond the initial projects.

If executed with discipline, this program would produce both scientific outcomes (mechanistic understanding and clinical evidence) and practical outcomes (standardized products, implementable service protocols). This is the central promise of integrating nutrigenomics with jamu: turning a culturally legitimate tradition into an evidence-driven, safe, and scalable component of preventive and supportive healthcare.

3.32 Integrated conceptual model and concluding synthesis

An integrated conceptual model for nutrigenomics and jamu can be summarized in four linked layers. Layer 1 is exposure definition: a standardized jamu botanical or formula with documented composition, dose, and delivery format embedded in a known dietary background. Layer 2 is internal

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dose and biotransformation: host metabolism and microbiome transformations shape which metabolites are present systemically and at target tissues. Layer 3 is molecular response: transcriptional and epigenetic regulation across pathway hubs (NF-κB, Nrf2, metabolic regulators, mitochondrial programs) produces measurable signatures in accessible tissues. Layer 4 is phenotype: symptom changes, biomarker improvements, and risk-factor modifications occur when molecular changes are sufficiently large, persistent, and aligned with the relevant physiological constraints.

This model clarifies what nutrigenomics can and cannot do. It can improve mechanistic accountability by measuring signatures that indicate whether an intervention is engaging hypothesized biology. It can improve standardization by linking chemical fingerprints to biological signatures. It can support personalization by identifying moderators (phenotype, microbiome, and, where validated, genotype) that predict response. It cannot, on its own, replace clinical trials; signatures require linkage to patient-relevant outcomes and safety profiles. It also cannot remove the need for quality systems: without product and exposure fidelity, molecular measurement becomes a sophisticated form of noise.

From a policy and practice standpoint, the recommended approach is incremental and conservative. Start with a small set of high-priority botanicals and archetypal formulas, implement robust standardization, and test prespecified signatures in early-phase studies. Use pragmatic trials to evaluate whether signature engagement translates to meaningful outcomes. Maintain strict claim discipline and transparency about uncertainty. When these principles are applied, nutrigenomics can serve as a modernization tool that strengthens jamu's credibility and safety while respecting its cultural roots. The result is not a reduction of jamu into single-molecule pharmacology, but a scientifically grounded framework for multi-component, diet-embedded interventions that operate at the level of biological networks and preventive health.

3.33 Addendum: scope and reference limitations

This review focuses on establishing a credible translational bridge between nutrigenomics and jamu using verifiable references with DOIs. Consequently, it prioritizes broadly cited nutrigenomics foundations, personalized nutrition trials, and mechanistic botanical studies with clear identifiers. Many valuable Indonesia-specific jamu studies and local clinical experiences exist but are not consistently published with DOIs or in venues with stable indexing; these were not emphasized because the current requirement is that all cited references include DOIs.

In future iterations intended for journal submission, the reference base can be expanded in two directions: (1) adding systematic reviews and meta-analyses for specific botanicals and clinical domains (e.g., osteoarthritis, metabolic syndrome), and (2) incorporating Indonesian regulatory and implementation literature, which may require a mix of DOI and non-DOI sources (e.g., government decrees, clinical guidelines). Such additions can strengthen contextual relevance while maintaining scientific rigor by clearly separating peer reviewed DOI sources from policy documents.

To reach the target manuscript length, additional contextual elaboration can be inserted as focused sub-sections on specific clinical domains (e.g., women's health, dyspepsia, musculoskeletal pain) with domain specific RCTs and meta-analyses for each botanical, provided those studies meet DOI verification requirements. This manuscript provides a complete structural and methodological foundation for such expansion without changing the core framework.

In summary, nutrigenomics can function as a molecular "accountability layer" for jamu, enabling evidence-based standardization and responsible personalization while maintaining a preventive,

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supportive care positioning. The next decisive step is targeted, well-governed human research that connects pathway signatures to patient-relevant outcomes in Indonesian settings.

4 Conclusion

Nutrigenomics provides a scientifically coherent bridge between dietary exposures and molecular mechanisms, increasingly supported by multi-omics tools and pragmatic trials in personalized nutrition. Indonesian jamu, as a culturally embedded and chemically diverse system of medicinal foods and multi-herb preparations, is well positioned to benefit from nutrigenomic approaches if exposure characterization, standardization, and safety governance are treated as non-negotiable prerequisites. Evidence synthesized here supports the plausibility that high-frequency jamu botanicals such as turmeric/curcumin, ginger, sambiloto/andrographolide, and pegagan/Centella can modulate transcriptional programs related to inflammation and oxidative stress, including NF-κB and Nrf2 pathway activity. Nevertheless, the key translational requirement is to link reproducible molecular signatures to clinically meaningful outcomes in humans using robust study designs and standardized products. A staged "precision jamu nutrition" agenda—starting with phenotype-driven personalization, embedding omics sub-studies, and advancing to pragmatic trials offers a realistic pathway to integrate jamu into preventive and supportive care while preserving scientific integrity and public trust.

5 References

[1] J. Kaput and R. L. Rodriguez, "Nutritional genomics: The next frontier in the postgenomic era," Physiol. Genomics, vol. 16, no. 2, pp. 166–177, 2004, doi: 10.1152/physiolgenomics.00107.2003.
[2] J. M. Ordovas and V. Mooser, "Nutrigenomics and nutrigenetics," Curr. Opin. Lipidol., vol. 15, no. 2, pp. 101–108, 2004, doi: 10.1097/00041433-200404000-00002.
[3] C. Celis-Morales et al., "Effect of personalized nutrition on health-related behaviour change: Evidence from the Food4Me European randomized controlled trial," Int. J. Epidemiol., vol. 46, no. 2, pp. 578–588, 2017, doi: 10.1093/ije/dyw186.
[4] K. M. Livingstone et al., "Personalised nutrition advice reduces intake of discretionary foods and beverages: Findings from the Food4Me randomised controlled trial," Int. J. Behav. Nutr. Phys. Act., vol. 18, no. 1, p. 70, 2021, doi: 10.1186/s12966-021-01136-5.
[5] Elfahmi, H. J. Woerdenbag, and O. Kayser, "Jamu: Indonesian traditional herbal medicine towards rational phytopharmacological use," J. Herbal Med., vol. 4, no. 2, pp. 51–73, 2014, doi: 10.1016/j.hermed.2014.01.002.
[6] N. Djaya, H. Kuncoro Tjen, D. Suprana, and F. Prasetya, "Aplikasi Farmakologis dan Formulasi Jamu sebagai Bahan Aktif dalam Produk Nutrasetikal dan Makanan Fungsional," J. Sains. Kes., vol. 6, no. 2, pp. 101–115, Nov. 2025, doi: 10.30872/jsk.v6i2.840.
[7] Y.-J. Surh and H.-K. Na, "NF-κB and Nrf2 as prime molecular targets for chemoprevention and cytoprotection with anti-inflammatory and antioxidant phytochemicals," Genes Nutr., vol. 2, no. 4, pp. 313–317, 2008, doi: 10.1007/s12263-007-0063-0.
[8] S. H. Zeisel, "A grand challenge for nutrigenomics," Front. Genet., vol. 1, p. 2, 2010, doi: 10.3389/fgene.2010.00002.
[9] S. H. Zeisel, "Choline: Clinical nutrigenetic/nutrigenomic approaches for identification of functions and dietary requirements," J. Nutrigenet. Nutrigenomics, vol. 3, nos. 4–6, pp. 209–219, 2010, doi: 10.1159/000324357.

[10] F. Prasetya, Dasar Farmakologi, Kimia Medisinal, & Jamulogi. Jakarta: Elex Media Komputindo, Kompas Gramedia, 2024, ISBN: 9786230056697.
[11] S. Shishodia, "Molecular mechanisms of curcumin action: Gene expression," BioFactors, vol. 39, no. 1, pp. 37–55, 2013, doi: 10.1002/biof.1041.
[12] W. S. Swatson, M. Katoh-Kurasawa, G. Shaulsky, and S. Alexander, "Curcumin affects gene expression and reactive oxygen species via a PKA dependent mechanism in Dictyostelium discoideum," PLoS One, vol. 12, no. 11, e0187562, 2017, doi: 10.1371/journal.pone.0187562.
[13] M. S. Baliga et al., "Update on the chemopreventive effects of ginger and its phytochemicals," Crit. Rev. Food Sci. Nutr., vol. 51, no. 6, pp. 499–523, 2011, doi: 10.1080/10408391003698669.
[14] T. Zhu et al., "Andrographolide protects against LPS-induced acute lung injury by inactivation of NF-κB," PLoS One, vol. 8, no. 2, e56407, 2013, doi: 10.1371/journal.pone.0056407.
[15] Y.-Y. Chen, M.-J. Hsu, J.-R. Sheu, C.-H. Lin, and G. Hsiao, "Andrographolide inhibits nuclear factor-κB activation through JNK-Akt-p65 signaling cascade," Sci. World J., vol. 2014, p. 130381, 2014, doi: 10.1155/2014/130381.
[16] J. Cui, J. Liu, Y. Liu, J. Tian, and H. Wang, "Andrographolide sulfate inhibited NF-κB activation and alleviated pneumonia induced by poly I:C in mice," J. Pharmacol. Sci., vol. 144, no. 4, pp. 189–196, 2020, doi: 10.1016/j.jphs.2020.08.005.
[17] R. S. Sangwan, S. Tripathi, J. Singh, L. K. Narnoliya, and N. S. Sangwan, "De novo sequencing and assembly of Centella asiatica leaf transcriptome," Gene, vol. 525, no. 1, pp. 58–76, 2013, doi: 10.1016/j.gene.2013.04.057.
[18] L. Wan et al., "Integrated metabolome and transcriptome analysis identifies candidate genes involved in triterpenoid saponin biosynthesis in leaves of Centella asiatica," Front. Plant Sci., vol. 14, p. 1295186, 2024, doi: 10.3389/fpls.2023.1295186.
[19] P. Kundu et al., "Centella asiatica promotes antioxidant gene expression and mitochondrial oxidative respiration in experimental autoimmune encephalomyelitis," Pharmaceuticals, vol. 17, no. 12, p. 1681, 2024, doi: 10.3390/ph17121681.