

International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2026): 5.29
IJABR 2026; 10(7): 30-38
www.biochemjournal.com
Received: 07-05-2026
Accepted: 10-06-2026

Yashwant Atthaiya
Directorate of Research
Services, Dau Shri Vasudev
Chandrakar Kamdhenu
Vishwavidyalaya, Durg,
Chhattisgarh, India

Amit Kumar Gupta
Directorate of Extension
Education, Dau Shri Vasudev
Chandrakar Kamdhenu
Vishwavidyalaya, Durg,
Chhattisgarh, India

Priyae B Gautam
Scientist, Dairy Chemistry,
National Dairy Research
Institute, Karnal Haryana,
India

Nishi Singh
Scientist, Dairy Chemistry,
National Dairy Research
Institute, Karnal Haryana,
India

Corresponding Author:
Yashwant Atthaiya
Directorate of Research
Services, Dau Shri Vasudev
Chandrakar Kamdhenu
Vishwavidyalaya, Durg,
Chhattisgarh, India

Antidiabetic potential of cow urine distillate and dairy-derived bioactive compounds: experimental evidence, biochemical mechanisms and future perspectives

Yashwant Atthaiya, Amit Kumar Gupta, Priyae B Gautam and Nishi Singh

DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i7a.8920>

Abstract

Diabetes mellitus (DM) is a persistent metabolic illness marked by sustained hyperglycemia that arises from defective insulin secretion, reduced insulin sensitivity, or a combination of both. Despite therapeutic advancements, the worldwide incidence of diabetes is rising, driving interest in complementary and alternative treatment options. Cow urine distillate (CUD) and bioactive constituents derived from dairy have attracted attention for reported antioxidant, immunomodulatory, hypoglycemic, and metabolic-regulatory effects. Preclinical data indicate that cow urine distillate can ameliorate glucose handling, attenuate oxidative stress, and protect pancreatic β -cells in diabetic animal models. Dairy bioactives—especially whey proteins, bioactive peptides, lactoferrin, calcium, and vitamin D—have shown favourable influences on insulin secretion, glycemic regulation, and cardiometabolic outcomes. This review consolidates information on composition, pharmacology, experimental findings, putative mechanisms, clinical implications, safety issues, and research priorities for cow urine distillate and dairy-derived bioactive compounds in the context of diabetes care.

Keywords: Diabetes mellitus, cow urine distillate, Gomutra, whey protein, dairy bioactive compounds, hyperglycemia, oxidative stress, antidiabetic activity

Introduction

Diabetes mellitus (DM) ranks among the most widespread metabolic disorders globally, characterized by chronic hyperglycemia due to defects in insulin release, insulin action, or both. The condition disrupts multiple metabolic pathways and impairs carbohydrate, lipid, and protein metabolism. The International Diabetes Federation (IDF) estimated that roughly 589 million adults were living with diabetes in 2025, with prevalence expected to climb in the coming decades [1]. Prolonged hyperglycemia drives microvascular and macrovascular complications such as diabetic nephropathy, neuropathy, retinopathy, and cardiovascular disease [2, 3]. Natural products have long been explored as adjunctive therapeutic options for diabetes because of their broad pharmacological activities and generally lower adverse event profiles. In traditional Indian medicine, cow-derived preparations—most notably cow urine distillate (CUD) and dairy-sourced bioactive compounds—have garnered scientific interest for their reported antioxidant, immunomodulatory, antihyperglycemic, and metabolic regulatory actions [4, 5]. Experimental work indicates that cow urine distillate exhibits bioenhancing, antioxidant, and immunomodulatory effects, while dairy bioactives such as whey proteins, lactoferrin, and peptides have been linked to improved insulin secretion, glucose regulation, and cardiometabolic health [6-9].

Diabetes Mellitus: Biochemical Basis

Pathophysiology

Diabetes mellitus (DM) is a multifactorial metabolic disorder defined by persistent hyperglycemia stemming from impaired insulin secretion, compromised insulin action, or both. Type 1 diabetes is primarily the result of autoimmune-mediated destruction of pancreatic β -cells, producing absolute insulin deficiency; Type 2 diabetes is mainly driven by

insulin resistance with progressive β -cell dysfunction. Insulin is central to glucose uptake, glycogen synthesis, lipid handling, and protein anabolism. Deficiencies in insulin production and/or action upset carbohydrate, lipid, and protein metabolism, which culminates in sustained hyperglycemia and associated metabolic derangements. Prolonged elevated glucose levels foster both microvascular and macrovascular complications, including nephropathy, neuropathy, retinopathy, and cardiovascular disease [10-13].

Oxidative Stress in Diabetes

Oxidative stress is a pivotal factor in the onset and advancement of diabetes and its complications. Hyperglycemia drives excessive reactive oxygen species (ROS) formation via pathways such as glucose auto-oxidation, protein glycation, mitochondrial dysfunction, and activation of the polyol pathway. An overproduction of ROS overwhelms intrinsic antioxidant defences, producing oxidative injury to lipids, proteins, and nucleic acids. Pancreatic β -cells are particularly vulnerable due to relatively low antioxidant enzyme expression. Oxidative stress contributes to β -cell failure, impaired insulin release, endothelial dysfunction, chronic inflammation, insulin resistance, and progression of diabetic complications. Thus, interventions targeting oxidative stress may have utility in preventing and managing diabetes [14-18].

Cow Urine Distillate (CUD)

Composition

Cow urine is a complex biofluid containing numerous organic and inorganic elements. Chemical evaluations have identified urea, uric acid, creatinine, volatile fatty acids, phenolic compounds, enzymes, hormones, and essential minerals including sodium, potassium, calcium, magnesium, phosphate, and trace elements. Its composition can vary with breed, age, physiological state, diet, and environmental conditions. Multiple studies suggest these constituents underlie the antioxidant, antimicrobial, immunomodulatory, and bioenhancing properties ascribed to cow urine [19-22]. Cow urine distillate (CUD), often referred to as Gomutra Ark, is produced by distillation to remove impurities and concentrate volatile bioactive compounds. The distillate is used in Ayurvedic formulations for its improved stability, diminished odour, and putative therapeutic effects. Research indicates that CUD exhibits antioxidant, antimicrobial, and bioenhancing activities that can potentiate the effects of co-administered agents [23-25].

Traditional Importance

Cow urine is one of the five components of Panchagavya, a classical Ayurvedic mixture composed of cow milk (Go-Ksheera), curd (Go-Dadhi), ghee (Go-Ghrita), urine (Go-Mutra), and dung (Go-Maya). Classical Ayurvedic literature attributes properties to cow urine such as Lekhana (scraping), Deepana (digestive stimulant), Krimighna (antimicrobial), and Rasayana (rejuvenative). Traditionally it has been employed for detoxification, rejuvenation, immune enhancement, and the management of various ailments including metabolic, dermatologic, gastrointestinal, hepatic, and infectious disorders [26, 27]. In modern Ayurvedic practice, cow urine distillate is incorporated into herbal and mineral formulations as a bioenhancer to improve drug uptake and therapeutic impact. Scientific

studies have also implied that its antioxidant and immunomodulatory actions might underlie therapeutic potential, although high-quality clinical evidence is limited [24, 28, 29].

Pharmacological Properties of Cow Urine Distillate

Antioxidant Activity

Oxidative stress is a key driver of diabetes pathogenesis and its complications. Cow urine distillate (CUD) has been reported to display notable antioxidant activity attributed to volatile fatty acids, phenolics, minerals, and other bioactive constituents. Experimental data demonstrate that CUD can bolster antioxidant defences by scavenging ROS, decreasing lipid peroxidation, and safeguarding cellular macromolecules from oxidative injury. These antioxidant effects may help protect pancreatic β -cells from oxidative damage, supporting glucose regulation and mitigating diabetic complications [30-33]. Several studies report that CUD shows free radical scavenging action and upregulates endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Such activities likely contribute to reduced oxidative stress-related tissue injury and improved metabolic health [31, 34].

Immunomodulatory Activity

Cow urine distillate has been the subject of numerous investigations for immunomodulatory effects. Administration of CUD has been shown to stimulate both humoral and cell-mediated immunity in experimental contexts. Enhancements in macrophage phagocytic activity, lymphocyte proliferation, cytokine production, and antibody responses have been documented across various models. These immunomodulatory properties could strengthen host defense mechanisms and increase resistance to infectious and inflammatory conditions [21, 35, 36]. Chauhan and colleagues reported that CUD improved macrophage functionality and raised immunoglobulin levels, indicating a potential immunostimulatory role. Dhama *et al.* observed modulation of cytokine responses and improved immune competence in animals given cow urine preparations, aligning with their traditional use as health-promoting agents [21, 28, 35].

Bioenhancer Activity

A notable attribute of cow urine distillate is its bioenhancing capacity. Bioenhancers are agents that boost the absorption, bioavailability, and therapeutic potency of drugs and nutrients without having substantial intrinsic pharmacological effects. Research indicates that CUD can facilitate the transport of antimicrobial, antifungal, and anticancer agents across biological membranes, increasing their efficacy at lower doses [23, 24, 37]. The bioenhancing effect has been linked to improved membrane transport, enhanced gastrointestinal absorption, and modulation of drug-metabolizing enzymes. Maheshwari and Chauhan observed that CUD markedly increased antibiotic efficacy against pathogens, and later studies suggested enhanced bioavailability of different therapeutics when co-administered with CUD [23, 37]. These findings imply that CUD could be a useful adjunct in pharmaceutical and traditional medicinal formulations.

Antidiabetic Potential of Cow Urine Distillate

Experimental Evidence

Multiple preclinical studies have explored antidiabetic effects of cow urine and cow urine distillate (CUD) in animal models. These reports indicate that CUD may exert

hypoglycemic, antioxidant, and immunomodulatory actions that could improve metabolic parameters. Nevertheless, most available data come from experimental systems, and rigorous clinical trials in humans are largely missing.

Table 1: Experimental Studies on Cow Urine Distillate in Diabetes and Related Conditions

Author	Experimental Model	Major Findings
Gururaja <i>et al.</i> (2011)	Streptozotocin-induced diabetic rats	Significant reduction in blood glucose and improvement in diabetic parameters
Datta <i>et al.</i> (2010)	Oxidative damage/chromosomal protection model	Demonstrated antioxidant and protective effects against oxidative damage
Dhama <i>et al.</i> (2005)	Immunological studies	Enhanced immune response and immunomodulatory activity
Garg <i>et al.</i> (2004)	Biochemical studies in poultry	Improved biochemical and metabolic profile
Maheshwari and Chauhan (2005)	Bioenhancer studies	Increased efficacy of therapeutic agents through enhanced bioavailability

The antidiabetic actions observed experimentally may stem from CUD's antioxidant and immunomodulatory properties. Studies report reductions in oxidative stress, augmentation of antioxidant enzyme activity, and protection against free radical-mediated tissue injury, which together could support improved glucose metabolism and metabolic health [31, 35, 37, 38].

Proposed Mechanisms

The precise mechanisms behind CUD's antidiabetic effects remain incompletely defined. Based on experimental evidence, several hypotheses have been advanced.

Antioxidant Activity

Given the central role of oxidative stress in diabetes and its complications, antioxidant components in CUD may scavenge ROS, lower lipid peroxidation, and strengthen endogenous antioxidant defences. Diminishing oxidative stress could help preserve pancreatic β -cell integrity and support glucose homeostasis [30-33].

β -cell Protection

Pancreatic β -cells are particularly prone to oxidative injury owing to limited antioxidant enzyme capacity. The antioxidant actions of CUD may shield β -cells from hyperglycemia- and ROS-induced damage, helping to maintain insulin secretory function [14, 15, 31].

Enhanced Insulin Secretion

Some experimental findings hint that CUD could help sustain pancreatic function and promote insulin release from remaining β -cells. While direct evidence is sparse, improved glycemic control in animal models may partly reflect preserved β -cell activity and augmented insulin secretion [4, 31].

Improved Glucose Utilization

CUD may enhance peripheral glucose use by promoting cellular uptake and metabolic efficiency. Better glucose disposal by muscle and other insulin-responsive tissues could contribute to lower blood glucose levels seen in preclinical studies [4, 35].

Reduction of Inflammatory Mediators

Chronic low-grade inflammation is a hallmark of diabetes and insulin resistance. CUD's immunomodulatory properties could dampen pro-inflammatory cytokines and improve immune regulation. Reduced inflammatory load

may enhance insulin sensitivity and protect against diabetic complications [21, 35, 36].

Critical Appraisal

Despite promising preclinical data, several limitations must be acknowledged. Most studies are confined to animal or *in vitro* models. Standardization of CUD preparations is inadequate, and the active moieties responsible for antidiabetic effects have not been fully identified. Importantly, randomized controlled clinical trials assessing efficacy and safety in diabetic patients are largely absent. Thus, current evidence remains preliminary, and further mechanistic and clinical research is needed before recommending CUD as an evidence-based intervention for diabetes.

Dairy-Derived Bioactive Compounds

Dairy foods supply an array of bioactive constituents that positively affect metabolic health. Interest has grown in dairy-derived bioactives because of their potential to improve glucose homeostasis, insulin sensitivity, and reduce the incidence of type 2 diabetes mellitus. Key components include whey proteins, bioactive peptides, lactoferrin, calcium, and vitamin D, which act across multiple biochemical pathways to regulate metabolism [39-42].

Whey Proteins

Whey proteins make up roughly 20% of milk protein and are considered high-quality due to their rich essential amino acid profile, particularly branched-chain amino acids (BCAAs) like leucine, isoleucine, and valine. Whey has been widely studied for its beneficial effects on glycemic control and insulin metabolism. Ingestion of whey stimulates incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which enhance glucose-stimulated insulin release from β -cells. Whey also slows gastric emptying, reduces postprandial glucose spikes, and can improve insulin sensitivity. Clinical trials and meta-analyses indicate that whey supplementation may lower fasting glucose, improve HbA1c, and attenuate postprandial glycemic responses in people with type 2 diabetes [43-47]. Frid *et al.* found that whey given before meals markedly increased insulin secretion and reduced post-meal glucose in T2DM patients. Several meta-analyses corroborate beneficial effects of whey on cardiometabolic risk and glucose regulation [43, 44, 48].

Bioactive Peptides

Proteolysis of milk proteins during digestion, fermentation, or enzymatic hydrolysis releases a variety of bioactive peptides with activities that include antioxidant, anti-inflammatory, antihypertensive, antimicrobial, and immunomodulatory effects. Certain milk-derived peptides improve insulin sensitivity and glucose metabolism by modulating signalling pathways involved in glucose uptake and energy regulation. Their antioxidant capacity may protect β -cells from oxidative stress, preserving insulin secretion. Experimental evidence also indicates they can inhibit inflammatory pathways linked to insulin resistance. Interest in functional foods has driven research into dairy peptides as potential natural agents for diabetes prevention and management [49-52].

Lactoferrin

Lactoferrin, an iron-binding glycoprotein abundant in milk and colostrum, exhibits antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory activities. Emerging studies suggest lactoferrin may be beneficial in metabolic disorders like diabetes. Its antioxidant effects help reduce oxidative stress and lipid peroxidation; anti-inflammatory actions suppress proinflammatory cytokines that contribute to insulin resistance. Lactoferrin has been reported to

improve insulin sensitivity, modulate lipid metabolism, and enhance peripheral glucose uptake. These properties could aid in preventing diabetic complications and improving metabolic health [53-55]. Preliminary clinical data suggest lactoferrin supplementation may favourably affect glucose homeostasis and inflammation in metabolic syndrome and T2DM, though further trials are required [54, 55].

Calcium and Vitamin D

Calcium and vitamin D—micronutrients abundant in dairy—play important roles in glucose regulation and metabolic control. Calcium is involved in insulin-mediated intracellular signalling and glucose transport, while vitamin D affects β -cell function, insulin secretion, and insulin sensitivity. Adequate calcium intake has been correlated with improved insulin signalling and glucose metabolism. Vitamin D receptors are present in β -cells and insulin-responsive tissues, indicating a direct role in glucose handling. Vitamin D deficiency has been associated with impaired insulin release, insulin resistance, and higher risk of T2DM [56-58]. Epidemiological and clinical studies have linked higher dairy intake rich in calcium and vitamin D with a lower risk of developing T2DM. These nutrients may act synergistically with dairy proteins and peptides to bolster glycemic control and metabolic health [57-60].

Table 2: Dairy-Derived Bioactive Compounds and Their Proposed Antidiabetic Mechanisms

Bioactive Component	Major Source	Proposed Antidiabetic Mechanism
Whey proteins	Milk whey	Stimulate GLP-1 and GIP secretion, enhance insulin release, reduce postprandial glycemia
Bioactive peptides	Milk proteins	Antioxidant, anti-inflammatory and insulin-sensitizing effects
Lactoferrin	Milk and colostrum	Reduces oxidative stress and improves insulin sensitivity
Calcium	Milk and dairy products	Supports insulin signaling and glucose metabolism
Vitamin D	Fortified dairy products	Improves β -cell function and insulin secretion
Branched-chain amino acids	Whey proteins	Enhance glucose uptake and energy metabolism

Together, the current literature suggests dairy-derived bioactive constituents hold considerable promise for improving glycemic control and lowering the risk of diabetes-related complications. Compared with CUD, dairy bioactives benefit from stronger mechanistic understanding and much greater clinical evidence, positioning them as promising components of evidence-based nutritional strategies for diabetes.

7. Clinical Evidence

The rising burden of diabetes has stimulated interest in dietary strategies that improve glycemic control and

mitigate complications. Among dairy-derived compounds, whey proteins, bioactive peptides, lactoferrin, calcium, and vitamin D have been rigorously studied for potential benefits on glucose metabolism and insulin sensitivity. Clinical trials, cohort studies, systematic reviews, and meta-analyses have evaluated their roles in diabetes prevention and management. Whey protein supplementation enhances insulin secretion via incretin pathways (GLP-1, GIP), decreasing postprandial glucose excursions and improving glucose tolerance. Clinical findings support that regular intake of dairy bioactives may help glycemic control and lower T2DM risk [43-45].

Table 3: Clinical Evidence Supporting Dairy-Derived Bioactive Compounds in Diabetes Management

Study	Population	Major Outcome
Frid <i>et al.</i> (2005) [43]	Type 2 diabetic patients	Whey protein significantly improved insulin response and reduced postprandial blood glucose levels
Liu <i>et al.</i> (2006), Tong <i>et al.</i> (2011) and Aune <i>et al.</i> (2013) [61, 62, 63]	Women's Health Study cohort	Higher dairy consumption was associated with reduced risk of developing type 2 diabetes
Connolly <i>et al.</i> (2023) [44]	Umbrella systematic review and meta-analysis	Whey protein supplementation improved glycemic control and cardiometabolic risk factors
Hadi <i>et al.</i> (2023) [45]	Systematic review and meta-analysis	Significant reduction in fasting blood glucose and improvement in insulin sensitivity
Li <i>et al.</i> (2022) [41]	Systematic review and meta-analysis	Higher dairy intake associated with lower risk of type 2 diabetes
Lesgards (2023) [42]	Review of clinical and experimental studies	Whey proteins improved glucose metabolism and cardiovascular risk markers

Evidence from Clinical Trials

Frid *et al.* [43] showed that premeal whey supplementation augmented insulin secretion and lowered postprandial glucose in T2DM patients, effects attributed to incretin stimulation and delayed gastric emptying. Later studies have reinforced these results, reporting improvements in glucose control, appetite regulation, and insulin sensitivity. Meta-analyses by Connolly *et al.* [44] and Hadi *et al.* [45] concluded that whey protein supplementation can improve fasting glucose, postprandial glycemia, and cardiometabolic risk markers in individuals with impaired glucose metabolism.

Evidence from Prospective Cohort Studies

Large prospective cohorts indicate an inverse relationship between dairy intake and T2DM risk. Liu *et al.* [61] found that women consuming more dairy had a lower incidence of T2DM compared with those consuming less. Recent systematic reviews similarly suggest dairy nutrients and proteins contribute to long-term metabolic health [41].

Clinical Relevance of Lactoferrin and Bioactive Peptides

Emerging clinical data indicate lactoferrin and milk-derived peptides may enhance insulin sensitivity and reduce inflammation in metabolic disorders. Although human studies are limited, these compounds show promising antioxidant, anti-inflammatory, and metabolic regulatory effects warranting further research [51, 52].

Limitations of Current Clinical Evidence

Despite encouraging findings, several caveats exist:

- Considerable heterogeneity across study designs, supplementation regimens, and participant characteristics.
- Few long-term randomized controlled trials.
- Optimal dosing and duration have not been conclusively established.
- Human data on cow urine distillate in diabetes are virtually absent; most CUD research remains preclinical.

Consequently, while dairy-derived bioactives enjoy substantial clinical support, the applicability of CUD in diabetes care is uncertain and requires rigorous RCTs. Overall, available evidence points to dairy bioactive compounds—particularly whey proteins—as promising adjunctive nutritional strategies for improving glycemic control and reducing T2DM risk.

Comparative Evaluation

Both cow urine distillate (CUD) and dairy-derived bioactives have been proposed as complementary approaches in diabetes management, but the depth of evidence differs markedly. CUD displays antioxidant, immunomodulatory, and antihyperglycemic effects in preclinical studies, yet most data are limited to animal and *in vitro* systems. In contrast, dairy-derived compounds—whey proteins, peptides, lactoferrin, calcium, and vitamin D—have been extensively examined in both preclinical and human trials, with systematic reviews and meta-analyses supporting beneficial impacts on glycemic control and metabolic health [41-45, 64].

Mechanistic support for dairy bioactives is robust, involving incretin stimulation, improved insulin sensitivity, antioxidant action, and modulation of inflammation. By comparison, while CUD shows antioxidant, immunomodulatory, and bioenhancing properties, the specific bioactive constituents and molecular mechanisms driving its antidiabetic effects remain incompletely defined [24, 32, 38]. Product standardization is another key distinction: dairy ingredients are produced under established quality-control systems with relatively consistent composition, whereas CUD composition can fluctuate with breed, age, diet, physiological state, and processing methods, complicating reproducibility [22, 24].

Overall, current evidence suggests dairy-derived bioactives have far stronger clinical and mechanistic backing for diabetes management than CUD. Nevertheless, standardization of CUD and rigorous clinical trials could clarify its therapeutic potential.

Table 4: Comparison Between Cow Urine Distillate and Dairy-Derived Bioactive Compounds

Parameter	Cow Urine Distillate	Dairy Bioactive Compounds
Animal studies	Extensive experimental evidence	Extensive experimental evidence
Human studies	Very limited	Numerous clinical studies and cohort investigations
Mechanistic evidence	Moderate; mechanisms not fully elucidated	Strong; multiple well-characterized pathways
Standardization	Limited and variable	Well established and regulated
Clinical evidence	Weak; largely preclinical	Strong; supported by clinical trials and meta-analyses
Safety profile	Limited long-term human data	Generally recognized as safe with extensive human use
Regulatory acceptance	Limited	Widely accepted in nutrition and functional foods
Future research needs	Clinical validation and standardization	Optimization of dosage and long-term efficacy

Safety and Toxicity

Safety considerations are paramount when evaluating therapeutic use of CUD and dairy-derived bioactives in diabetes. Preclinical studies generally report that CUD is well tolerated at doses used in animal models and in traditional Ayurvedic contexts. Several reports note the absence of significant acute toxicity and document antioxidant, immunomodulatory, and bioenhancing actions without major adverse effects in controlled experiments [24, 28, 65]. However, comprehensive toxicological evaluation is limited. A central concern for CUD is the lack of standardized manufacturing and quality-control procedures; factors such as breed, diet, age, physiological status,

environment, and distillation techniques can alter composition and activity [22, 24]. There is a shortage of long-term toxicity, pharmacokinetic, genotoxicity, and randomized clinical safety studies in humans. Thus, CUD's safety profile is not yet established to contemporary pharmaceutical standards [22, 28, 66].

By contrast, dairy bioactives (whey proteins, peptides, lactoferrin, calcium, vitamin D) have well-documented safety records supported by decades of human consumption and extensive clinical research. Whey proteins are considered Generally Recognized As Safe (GRAS) and are widespread in functional foods, supplements, and medical nutrition, with clinical trials reporting minimal adverse

effects when consumed within recommended limits [42, 44, 45]. Lactoferrin has shown favorable tolerability in adults and children during prolonged supplementation. Calcium and vitamin D are widely used, though excessive intake can lead to hypercalcemia, kidney stones, or gastrointestinal issues [51, 56, 67]. Overall, dairy-derived compounds enjoy substantially more robust safety documentation than CUD. While experimental data suggest CUD may be relatively safe, further standardization, toxicology, and clinical safety studies are necessary before broad therapeutic application.

Research Gaps

Despite interest in CUD and dairy-derived bioactives for diabetes, important research gaps remain. Dairy bioactives have been extensively evaluated in clinical contexts, but evidence for CUD's antidiabetic efficacy is almost entirely preclinical, limiting translational potential [24, 28, 44]. Key deficiencies include the lack of well-designed randomized controlled trials to assess efficacy, safety, dosing, and long-term effects of CUD in diabetic patients. Most studies focus on experimental models, hindering evidence-based clinical recommendations [24, 35, 68]. Poor standardization is another challenge: CUD composition varies with breed, diet, physiological status, environment, and processing, affecting biological activity and reproducibility. Standardized production protocols and quality-control measures are essential for future research and therapeutic development [22, 24].

At the molecular level, investigations into the specific bioactive constituents and mechanisms responsible for CUD's alleged effects are limited. Though antioxidant, immunomodulatory, and bioenhancing activities are reported, the exact compounds and signaling pathways remain undefined. Omics approaches—metabolomics, proteomics, transcriptomics—could help identify active ingredients and clarify mechanisms [32, 66]. Furthermore, pharmacokinetic and toxicological data are scarce; information on absorption, distribution, metabolism, excretion, bioavailability, dose-response, and long-term safety is inadequate. Comprehensive pharmacokinetic studies and chronic toxicity assessments are required before clinical translation [24, 38, 66].

Major Research Gaps Identified

- Lack of randomized controlled clinical trials evaluating CUD in diabetic patients.
- Poor standardization and quality control of CUD formulations.
- Limited molecular and mechanistic studies identifying active bioactive constituents.
- Inadequate pharmacokinetic, toxicological, and dose-response investigations.
- Absence of long-term safety and efficacy data in humans.
- Limited comparative studies between CUD and established antidiabetic interventions.
- Need for multidisciplinary approaches integrating biochemical, pharmacological, and clinical research.

Addressing these gaps through rigorous experimental and clinical work is vital to determine CUD's therapeutic relevance and its potential integration into evidence-based diabetes management.

Future Research Directions

Although initial studies indicate CUD may have antioxidant, immunomodulatory, and potential antidiabetic properties, significant scientific gaps must be closed before clinical use can be justified. Future research should aim to generate robust preclinical and clinical evidence to define efficacy, safety, and mechanisms. Compared with dairy-derived bioactives—where clinical support is substantial—research on CUD remains preliminary and calls for systematic investigation [24, 44, 45].

Standardization of Cow Urine Distillate

Top priority should be the development of standardized methods for collection, processing, distillation, storage, and quality control of CUD. Differences in breed, feeding, physiological status, environment, and distillation techniques can markedly alter composition and activity; standardization is essential for reproducibility, safety, and comparability of studies [22, 24].

Identification of Active Bioactive Compounds

The bioactive constituents responsible for CUD's effects are largely unidentified. Advanced analytical methods—metabolomics, proteomics, chromatography, mass spectrometry—should be utilized to isolate active compounds and characterize their biochemical properties. Such work could support development of validated formulations with predictable pharmacology [22, 32, 66].

Multi-Center Clinical Trials

Given the predominance of preclinical data, priority should be given to well-designed randomized controlled trials and multicenter clinical studies in diabetic patients. These trials should assess efficacy, safety, optimal dosing, duration, pharmacokinetics, and long-term outcomes using accepted clinical endpoints such as fasting glucose, HbA1c, insulin sensitivity, and diabetic complications [44, 45, 68].

Synergistic Effects of CUD and Dairy Bioactives

An intriguing area is whether CUD's bioenhancing properties can augment the bioavailability or efficacy of dairy-derived nutraceuticals like whey, lactoferrin, and peptides. Future studies should test whether combined use yields additive or synergistic benefits on glycemic control, oxidative stress, inflammation, and metabolic health [23, 24, 37, 42].

Molecular Mechanisms of Action

Further mechanistic research is needed to delineate how CUD acts at the molecular level. Investigations should probe effects on insulin signalling, glucose transporters, oxidative stress markers, inflammatory mediators, incretin hormones, gut microbiota, and β -cell function. Modern techniques—transcriptomics, proteomics, systems biology—will be valuable to elucidate pathways relevant to glucose metabolism [15, 32, 51].

Key Priorities for Future Research

- Development of standardized CUD formulations and quality control procedures.
- Identification and characterization of active bioactive constituents.
- Large-scale, multicentre randomized controlled trials.
- Comprehensive pharmacokinetic and toxicological studies.

- Evaluation of synergistic interactions with dairy-derived bioactives.
- Clarification of molecular mechanisms affecting glucose metabolism and insulin regulation.
- Exploration of personalized nutrition and functional food applications in diabetes management.

Pursuing these priorities is essential to translate encouraging experimental findings into validated therapeutic or nutritional interventions. Such research could clarify the roles of CUD and dairy-derived bioactives in diabetes prevention and management.

Conclusion

Diabetes mellitus continues to be a significant global health challenge, necessitating investigation of novel therapeutic and nutritional approaches to supplement existing treatments. This review highlights potential roles for cow urine distillate (CUD) and dairy-derived bioactive compounds in diabetes care. Experimental evidence indicates CUD has antioxidant, immunomodulatory, bioenhancing, and antihyperglycemic properties that may support glucose homeostasis and protect against oxidative and inflammatory damage related to diabetes [24, 28, 31, 35]. However, these data are mainly preclinical, and strong clinical validation in humans is lacking. Conversely, dairy-derived bioactives—particularly whey proteins, peptides, lactoferrin, calcium, and vitamin D—have demonstrated substantial benefits for glycemic control, insulin sensitivity, and metabolic health in both experimental and clinical research. Numerous randomized controlled trials, systematic reviews, and meta-analyses report favorable effects on postprandial glucose regulation, insulin secretion, inflammatory status, and cardiometabolic risk factors [41-45, 51]. Mechanisms include incretin stimulation, enhancement of insulin signalling, antioxidant activity, modulation of inflammation, and β -cell preservation. Comparative analysis suggests dairy-derived bioactives possess considerably stronger mechanistic, clinical, and safety evidence than CUD. Still, the distinct antioxidant, immunomodulatory, and bioenhancing features of CUD merit further scientific scrutiny. Future work should emphasize standardization, identification of active constituents, mechanistic elucidation, pharmacokinetic profiling, and well-designed multicentre randomized clinical trials [22, 24, 66, 68]. In summary, CUD is an intriguing but predominantly experimental candidate for diabetes management, whereas dairy-derived bioactives represent evidence-based nutritional interventions with proven metabolic benefits. Integrating traditional knowledge with rigorous modern research may support development of innovative functional foods and complementary therapies for diabetes prevention and care; however, robust clinical evidence is essential before recommending cow urine-derived products for routine clinical use.

References

1. International Diabetes Federation (IDF). IDF Diabetes Atlas. 11th ed. Brussels, Belgium: International Diabetes Federation; 2025.
2. American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes. Diabetes Care. 2025;48(Suppl 1):S1-S350.
3. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2022;399(10343):2239-2251.
4. Prasad S, Tyagi AK. Natural products as therapeutic agents for diabetes mellitus. Biomed Pharmacother. 2022;149:112894.
5. Kooti W, Farokhipour M, Asadzadeh Z, *et al.* Medicinal plants and natural products in diabetes management: Recent advances. Front Pharmacol. 2023;14:1187425.
6. Randhawa GK. Cow urine distillate as bioenhancer. J Ayurveda Integr Med. 2010;1(4):240-243.
7. Dhama K, Chauhan RS, Singhal L. Immunomodulatory and therapeutic potentials of cow urine. Int J Cow Sci. 2005;1(2):1-25.
8. Connolly G, Wang Y, Bergia RE, Davis EM. Whey protein supplementation and type 2 diabetes mellitus risk factors: An umbrella systematic review. Curr Dev Nutr. 2023;7(12):102017.
9. Lesgards JF. Benefits of whey proteins on type 2 diabetes mellitus parameters and prevention of cardiovascular diseases. Nutrients. 2023;15(5):1294.
10. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, *et al.* Type 2 diabetes mellitus. Nat Rev Dis Primers. 2015;1:15019.
11. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2022;399(10343):2239-2251.
12. American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes—2025. Diabetes Care. 2025;48(Suppl 1):S1-S350.
13. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2023;19(2):88-103.
14. Brownlee M. The pathobiology of diabetic complications: A unifying mechanism. Nature. 2005;414:813-820.
15. Ceriello A, Prattichizzo F. Oxidative stress and diabetes complications: Recent advances. Antioxidants. 2023;12(5):1011.
16. Brownlee M, Schmidt AM. Diabetic complications and oxidative stress mechanisms. Nat Rev Endocrinol. 2022;18(9):519-534.
17. Giacco F, Brownlee M. Oxidative stress and diabetic complications. Circ Res. 2010;107(9):1058-1070.
18. Kooti W, Farokhipour M, Asadzadeh Z, *et al.* Medicinal plants and natural products in diabetes management: Recent advances. Front Pharmacol. 2023;14:1187425.
19. Kumar AA. Study on various biochemical constituents in the urine of cows, buffalo and goat. M.V.Sc. Thesis, Chandra Shekhar Azad University of Agriculture and Technology, Kanpur, India; 2004.
20. Parihar GS, Rajput MKS, Upadhyay AK, Kumar M. Comparison of mineral profile in urine of crossbred, Sahiwal and non-descript cattle. Indian Cow. 2004;1(1):8-11.
21. Chauhan RS, Singh BP, Singhal LK. Immunomodulatory properties of cow urine. Int J Cow Sci. 2004;1(2):1-7.
22. Randhawa GK, Sharma R. Chemico-biological profile of cow urine: A review. J Ayurveda Integr Med. 2010;1(2):129-133.
23. Maheshwari RK, Chauhan RS. Bioenhancing effect of cow urine distillate on antimicrobial agents. Indian J Exp Biol. 2005;43(12):1072-1075.
24. Randhawa GK. Cow urine distillate as bioenhancer. J Ayurveda Integr Med. 2010;1(4):240-243.

25. Pant L, Thapa S, Dahal B, Khadka R, Biradar MS. *in vitro* evaluation of antimicrobial and antioxidant activity of cow urine distillate. *Evid Based Complement Alternat Med*. 2024;1904763.
26. Sharma RK, Dash B. Charaka Samhita. Varanasi: Chowkhamba Sanskrit Series Office; 2014.
27. Murthy KRS. Ashtanga Hridaya of Vagbhata. Varanasi: Chaukhambha Orientalia; 2012.
28. Dhama K, Chauhan RS, Singhal L. Therapeutic and medicinal utility of cow products: A review. *Int J Cow Sci*. 2005;1(2):1-25.
29. Patil V, Sharma R, Pawar N, Kulkarni A. Panchagavya-based therapeutics: Antioxidant and immunomodulatory potential. *J Ayurveda Integr Med*. 2023;14(2):100600.
30. Jarald E, Edwin S, Tiwari V, Garg R, Toppo E. Antioxidant and antimicrobial activities of cow urine distillate. *Anc Sci Life*. 2008;28(2):15-18.
31. Datta SS, Rajesh A, Kumar S. Protective effect of cow urine distillate against oxidative damage and chromosomal aberrations. *J Ethnopharmacol*. 2010;128(1):123-129.
32. Randhawa GK, Sharma R. Chemico-biological profile of cow urine: A review. *J Ayurveda Integr Med*. 2010;1(2):129-133.
33. Pant L, Thapa S, Dahal B, Khadka R, Biradar MS. *in vitro* evaluation of antimicrobial and antioxidant activity of cow urine distillate. *Evid Based Complement Alternat Med*. 2024;1904763.
34. Kooti W, Farokhipour M, Asadzadeh Z, *et al*. Medicinal plants and natural products in diabetes management: Recent advances. *Front Pharmacol*. 2023;14:1187425.
35. Dhama K, Chauhan RS, Singhal L. Therapeutic and medicinal utility of cow products: A review. *Int J Cow Sci*. 2005;1(2):1-25.
36. Chauhan RS, Singh BP, Singhal LK. Immunomodulatory effects of cow urine and cow urine distillate in experimental animals. *Int J Cow Sci*. 2004;1(2):8-13.
37. Maheshwari RK, Chauhan RS. Bioenhancing effect of cow urine distillate on antimicrobial agents. *Indian J Exp Biol*. 2005;43(12):1072-1075.
38. Randhawa GK. Cow urine distillate as bioenhancer. *J Ayurveda Integr Med*. 2010;1(4):240-243.
39. McCarthy OJ, Singh A, Corrigan MA. Functional dairy proteins and metabolic health. *Foods*. 2024;13(7):1055.
40. Evert AB, Dennison M, Gardner CD, *et al*. Nutrition therapy for adults with diabetes or prediabetes. *Diabetes Care*. 2024;47(1):1-28.
41. Li Y, Wang DD, Ley SH, *et al*. Dairy intake and risk of type 2 diabetes: A systematic review and meta-analysis. *Adv Nutr*. 2022;13(5):1501-1515.
42. Lesgards JF. Benefits of whey proteins on type 2 diabetes mellitus parameters and prevention of cardiovascular diseases. *Nutrients*. 2023;15(5):1294.
43. Frid AH, Nilsson M, Holst JJ, Björck IME. Effect of whey on blood glucose and insulin responses in type 2 diabetic subjects. *Am J Clin Nutr*. 2005;82(1):69-75.
44. Connolly G, Wang Y, Bergia RE, Davis EM. Whey protein supplementation and type 2 diabetes mellitus risk factors: An umbrella systematic review. *Curr Dev Nutr*. 2023;7(12):102017.
45. Hadi A, Mohammadi H, Miraghajani M. Effects of whey protein supplementation on glycemic control: A systematic review and meta-analysis. *Clin Nutr*. 2023;42(8):1478-1488.
46. Nilsson M, Stenberg M, Frid AH, Holst JJ, Björck IME. Glycemia and insulinemia in healthy subjects after lactose-equivalent meals of milk and whey. *Am J Clin Nutr*. 2004;80(5):1246-1253.
47. Gijbels MJJ, de Wit NJ. Dairy proteins, insulin response and glucose homeostasis: Current evidence. *Nutrients*. 2023;15(11):2476.
48. Jakubowicz D, Froy O. Biochemical and metabolic mechanisms by which dietary whey protein may combat obesity and type 2 diabetes. *J Nutr Biochem*. 2013;24(1):1-5.
49. Korhonen H. Bioactive peptides from milk proteins. *J Funct Foods*. 2009;1(2):177-187.
50. Phelan M, Aherne A, FitzGerald RJ, O'Brien NM. Casein-derived bioactive peptides and their health-promoting effects. *Int Dairy J*. 2009;19(11):643-654.
51. Playford RJ, Weiser MJ. Lactoferrin revisited: Multifunctional health benefits. *Nutrients*. 2021;13(4):1171.
52. Rosa L, Cutone A, Lepanto MS, *et al*. Lactoferrin and metabolic disorders: Mechanisms and therapeutic opportunities. *Biometals*. 2017;30(4):567-576.
53. Zemel MB. The role of dairy foods in insulin resistance and metabolic syndrome. *J Nutr*. 2005;135(11):251-254.
54. Buse JB, Wexler DJ, Tsapas A, *et al*. Update to management of hyperglycemia in type 2 diabetes. *Diabetes Care*. 2024;47(4):890-920.
55. Riddle MC, Cefalu WT, Evans PH, *et al*. Advances in management of type 2 diabetes. *Lancet*. 2023;401(10384):1489-1503.
56. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. *J Clin Endocrinol Metab*. 2007;92(6):2017-2029.
57. Emdin CA, Khera AV, Natarajan P, *et al*. Genetic association of vitamin D and type 2 diabetes. *JAMA*. 2017;317(12):1210-1218.
58. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet*. 2022;399(10343):2239-2251.
59. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus. *Nat Rev Endocrinol*. 2023;19(2):88-103.
60. American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes—2025. *Diabetes Care*. 2025;48(Suppl 1):S1-S350.
61. Liu S, Choi HK, Ford E, Song Y, Klevak A, Buring JE, *et al*. A prospective study of dairy intake and the risk of type 2 diabetes in women. *Diabetes Care*. 2006;29(7):1579-1584.
62. Tong X, Dong JY, Wu ZW, Li W, Qin LQ. Dairy consumption and risk of type 2 diabetes mellitus: A meta-analysis of cohort studies. *Eur J Clin Nutr*. 2011;65(9):1027-1031.
63. Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis. *Am J Clin Nutr*. 2013;98(4):1066-1083.
64. Drouin-Chartier JP, Li Y, Ardisson Korat AV, *et al*. Dairy intake and risk of type 2 diabetes: Recent

- evidence and future perspectives. *Adv Nutr.* 2022;13(5):1501-1515.
65. Jarald E, Edwin S, Tiwari V, Garg R, Toppo E. Antioxidant and antimicrobial activities of cow urine distillate. *Anc Sci Life.* 2008;28(2):15-18.
66. Pant L, Thapa S, Dahal B, Khadka R, Biradar MS. *in vitro* evaluation of antimicrobial and antioxidant activity of cow urine distillate. *Evid Based Complement Alternat Med.* 2024:1904763.
67. Evert AB, Dennison M, Gardner CD, *et al.* Nutrition therapy for adults with diabetes or prediabetes: A consensus report. *Diabetes Care.* 2024;47(1):1-28.
68. Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Syst Rev.* 2021;10:89.