Research Article

Dietary Protein Level and Purine Derivative Excretion in Ruminants: A Systematic Review and Meta-Analysis.

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Abstract | Purine derivatives, the by-products of microbial metabolism, serve as key indicators of microbial protein synthesis in ruminants. Among these, allantoin is the predominant purine derivative excreted in urine and reflects the extent of microbial protein production. Its concentration is positively correlated with organic matter intake and the proportion of concentrate in the diet, both of which enhance microbial biomass yield. Numerous studies have demonstrated that higher allantoin levels indicate greater microbial protein synthesis.The present study aimed to evaluate the effect of protein-rich diets on purine derivative excretion in ruminants through a meta-analysis. A total of 32 Scopus-indexed studies were screened, and 11 qualified datasets were compiled into a comprehensive database. Data were analyzed using a random-effects model in OpenMEE software. Purine derivatives were classified as the experimental variables, while corresponding lower-protein or protein-free diets served as controls. Publication bias in the primary parameters of purine derivative excretion (allantoin, uric acid, xanthine + hypoxanthine) was assessed using funnel plots.The meta-analysis revealed a significant difference between high-protein and low- or protein-free diets with respect to allantoin levels in ruminants ($P<0.001$). Similarly, uric acid levels differed significantly between dietary groups ($P = 0.048$). Overall, the findings suggest that feeding ruminants low-protein diets reduced excessive protein degradation in the rumen, whereas high-protein diets may alter purine metabolism and microbial efficiency.

Keywords | Excretion, feed, meta-analysis, purine, protein, ruminant

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INTRODUCTION

Modern concepts in ruminant ration formulation must consider the balance of protein and energy to support maximum rumen microbial protein production in addition to the supply of feed protein that escapes rumen degradation (Firkins 2021; Moorby and Fraser 2021; Lima *et al*., 2023; Yunilas *et al*., 2023; Febrina *et al*., 2025). However, the expectation that increasing dietary protein will always increase microbial protein synthesis (MPS) and urinary purine derivative (PD) excretion is not necessarily valid across study contexts, because microbial capture of nitrogen depends on concurrent fermentable energy supply and nitrogen–energy synchrony. When rumen-degradable nitrogen is oversupplied relative to fermentable energy, ammonia capture may decline and nitrogen is diverted to loss pathways rather than microbial biomass formation, implying a non-linear (threshold) response beyond an optimal range (Santos *et al*., 2021).

The ability of rumen microbes to synthesize their cell protein depends on the substrate being fermented and the rate of microbial growth (Febrina *et al*., 2017a; Amin and Mao 2021; Liu *et al*., 2021). Microbial Protein Synthesis (MPS) is the largest contributor to total protein available and absorbed in the duodenum (Febrina *et al*., 2016; Putri *et al*., 2021; Rosmalia *et al*., 2022). Several methods are used to estimate microbial protein synthesized in the rumen such as microbial markers (2,4 diaminopimelic acid: DAPA and purine bases) (Gresner *et al*., 2021; Mahanani *et al*., 2021a; Lima *et al*., 2023; Mahboobi *et al*., 2023), tracer methods using isotopes such as 15N (Lima *et al*., 2023), 32P and 35S (Mahboobi *et al*., 2023) and PD excretion through urine (Chen *et al*., 1990; Kazemi-Bonchenari *et al*., 2022; Del Valle *et al*., 2023; Nichols *et al*., 2024) are the most commonly used methods (Castro-Montoya *et al*., 2016; Wu *et al*., 2021).

Purine derivatives are by-products of purine base and nucleic acid metabolism, and serve as a useful index for estimating the quantity of microbial protein synthesised within the rumen. Nucleic acids exiting the rumen originate from microbes, as feed contains only a limited amount of purines that undergo extensive degradation due to rumen microbial fermentation (Crawford *et al*., 2020; Keum *et al*., 2024). Absorbed purine nucleic acids are further degraded and subsequently eliminated through urine in the form of their derivatives, including allantoin, xanthine, hypoxanthine, and uric acid (Chen *et al*., 1990; Lestari *et al*., 2021; Sousa *et al*., 2022; Mahboobi *et al*., 2023). Purine derivatives entering the bloodstream arise not only from absorption but also from the breakdown of nucleic acid tissues, known as basal (endogenous) purine derivatives (Putri *et al*., 2021). In cattle, basal purine derivative excretion is three times higher than in sheep (Silva *et al*., 2021; Valizadeh *et al*., 2021).

In ruminants, allantoin is the main product of purine catabolism and the largest amount of purine derivatives in urine, so that it can be used as an indicator of the amount of microbial protein formation (Harun *et al*., 2017). Allantoin, the primary product of purine catabolism, stands as the most abundant purine derivative in ruminant urine, making it a valuable indicator of microbial protein synthesis (Molaei *et al*., 2021). Allantoin constitutes 80–85% of endogenous purine derivatives in urine, while uric acid accounts for 15–20%, with proportions remaining relatively constant yet varying among animals (Chen *et al*., 1990).

Purine derivatives concentration is closely linked to organic matter intake, as digested organic matter within the rumen serves as the energy source for rumen microbial formation (Mahboobi *et al*., 2023). Elevated organic matter consumption leads to increased rumen microbial biomass production, consequently raising the concentration of excreted purine derivatives (Febrina *et al*., 2017b; Newbold and Ramos-Morales 2020; Gonzalez-Ronquillo *et al*., 2021). Urinary excretion of purine derivatives, particularly allantoin, exhibits a positive correlation with nucleic acid supplementation (Chen *et al*., 1990) and urea-ammoniated feed administration (Müller *et al*., 2021; Silva *et al*., 2021; Valizadeh *et al*., 2021; Ortolani *et al*., 2022). Increasing concentrate levels in rations also enhances allantoin concentration, with high allantoin levels indicative of substantial microbial protein formation (Valizadeh *et al*., 2021; Ningrum *et al*., 2022). Rumen protozoa play a crucial role in nitrogen utilization, as evidenced by the correlation between plasma allantoin concentration and total purine derivative excretion in sheep (Solomon *et al*., 2022; Jalayerinejad *et al*., 2024).

Nevertheless, PD output is not governed by crude protein supply alone; it is highly modulated by the degradability profile of protein (RDP vs RUP) and fermentable carbohydrate supply, which determine whether absorbed nitrogen is incorporated into microbial nucleic acids or lost as ammonia/urea. Recent evidence shows that altering the rumen-degradable starch to rumen-degradable protein ratio changes fermentation characteristics and microbial protein synthesis, supporting the concept that energy–nitrogen synchrony can shift the expected PD response even at comparable protein intake (Chen *et al*., 2022). Therefore, it is plausible that beyond an optimal point, additional dietary protein becomes "detrimental" to PD output not because protein is intrinsically harmful, but because oversupply without matching energy reduces microbial nitrogen capture efficiency and thus microbial purine flow (Santos *et al*., 2021; Chen *et al*., 2022).

Several studies have evaluated how various factors influence purine excretion. For example, Nguyen and Nguyen (2021) examined differences in purine excretion among herbivorous species. Valizadeh *et al*. (2021) investigated the influence of the ratio of rumen undegradable protein to rumen degradable protein on purine excretion, reporting an increase in purine-based measurements as the ratio increased. Ortolani *et al*., (2022) studied the effects of feeding, fasting, and re-feeding conditions on purine excretion. Mahanani *et al*. (2021) evaluated the role of sex in purine excretion, while Gonzalez-Ronquillo *et al*. (2021) demonstrated that the form in which forages are offered, either as hay or silage, can influence purine derivatives. Finally, Purwati *et al*. (2024) reported on the influence of breed differences on purine excretion. However, there are limited studies evaluating how high- and low-protein diets affect purine excretion, as well as on identifying patterns and synchrony among studies conducted in different locations and at different times using meta-analytical means. Importantly, while the prevailing premise states that PD excretion correlates positively with protein intake, our meta-analytic evidence indicates that higher-protein diets can be associated with lower PD excretion in certain contexts creating a central paradox that motivates this study and must be explicitly tested.

Accordingly, this paper aims to evaluate the relationship between protein-rich feeds and purine derivative excretion in ruminants using a meta-analysis, with the explicit working hypothesis that the protein–PD relationship may be context-dependent and potentially non-linear (i.e., increasing up to an optimal point and decreasing/plateauing under oversupply or asynchrony), while also quantifying pooled effects and between-study variability (Galyean and Tedeschi, 2024).

MATERIALS AND METHODS

Ethical approval

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA protocol (Page et al., 2021). Ethical approval was not required since all data was obtained from previously published studies.

Search strategy

A systematic and comprehensive literature search was conducted in Scopus and Web of Science to identify studies assessing the relationship between dietary protein supply and urinary purine derivative excretion in ruminants. The search strategy combined free-text terms using Boolean operators as follows: (“ruminant” OR “cattle” OR “sheep” OR “goat”) AND (“purine derivatives” OR “allantoin” OR “uric acid” OR “xanthine” OR “hypoxanthine”) AND (“protein feed” OR “dietary protein” OR “protein level” OR “protein supplementation”). No restriction was imposed on publication year; however, only peer-reviewed journal articles published in English were eligible. The reference lists of included articles were also screened to identify additional studies.

The PRISMA 2020 study selection process is summarized in Figure 1. A total of 475 records were identified through database searching. Duplicate records were removed using Mendeley Reference Manager (n = 406), leaving 69 unique records for title/abstract screening. During screening, 37 records were excluded because they were unrelated to purine derivatives, involved non-ruminant species, or were review/non-original publications. The full texts of the remaining 32 reports were assessed for eligibility; 21 reports were excluded with reasons (incomplete numerical data, no defined dietary-protein comparison/control group, or incompatible intervention). Ultimately, 11 studies met the inclusion criteria and were included in the quantitative meta-analysis.

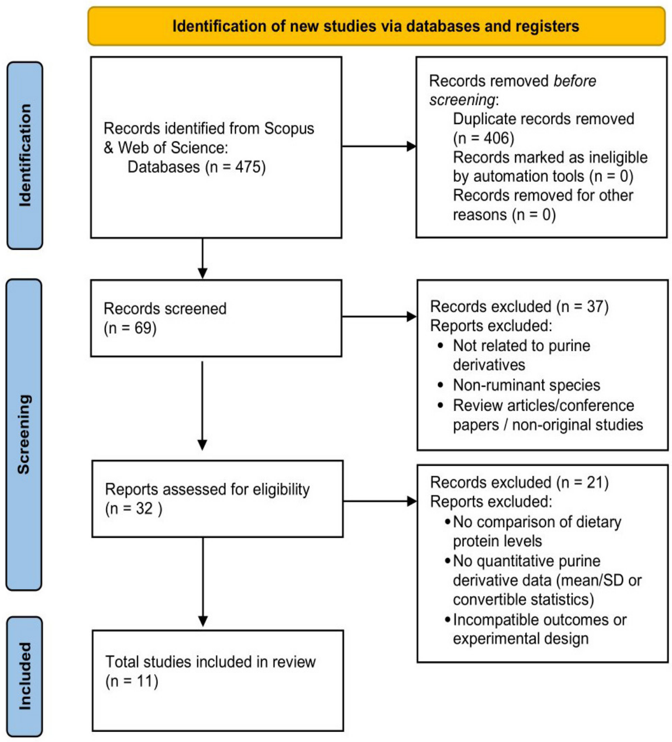

Figure 1: flow chart artical with PRISMA protocol

Inclusion and exclusion criteria

Studies were included if they (i) involved ruminant species (cattle, sheep, goats, or other domesticated ruminants), (ii) investigated the impact of dietary protein level/nitrogen supply on urinary purine derivatives (allantoin, uric acid, xanthine, and/or hypoxanthine), and (iii) reported sufficient quantitative data (mean, standard deviation/standard error, and sample size) to compute standardized effect sizes. Eligible studies were required to include at least two dietary conditions that differed in protein level (e.g., higher vs. lower protein, protein supplementation vs. reduced protein) with a clearly defined comparator.

Studies were excluded if they were review papers, abstracts, or non-peer-reviewed publications; lacked essential numerical information (mean ± SD/SE and n); did not specify diet composition or comparator definitions; or focused primarily on non-dietary interventions. Of the 32 full-text reports assessed, 21 were excluded due to incomplete numerical data (n = 10), absence of a defined dietary-protein comparator/control group (n = 6), or incompatible intervention/outcome design (n = 5). Details of included studies are presented in Table 1.

Definition of groups and data extraction

The included studies were categorized based on experimental conditions into high-protein diets, low-protein diets, protein-free diets, and fasting conditions (animals withheld from feed but not water). To avoid conceptual and physiological confounding, fasting trials were treated as a distinct subgroup and were not pooled with fed low-protein/protein-free conditions. Primary meta-analyses focused on fed comparisons (higher-protein vs lower-protein/protein-free); while fasting comparisons were evaluated separately as subgroup/sensitivity analyses.

Data extraction was performed manually using Microsoft Excel 2019. Extracted variables included: study ID (author, year), ruminant species/physiological state, diet descriptions (including protein level where reported), outcome type (allantoin, uric acid, xanthine, hypoxanthine, total PD), sample size (n), mean, and SD/SE for each group, and sampling time/duration. The unit of analysis was an independent comparison (effect size) per outcome. Each row in the final dataset represented one comparison (treatment vs comparator) for one outcome, including the computed Hedges' g and its variance.

Handling multi-arm studies and repeated time points: (i) If a study reported more than two protein levels, we used the contrast between the highest and lowest protein levels under fed conditions. When multiple contrasts shared a common control, the control group sample size was divided across contrasts to avoid double-counting. (ii) If multiple time points were reported, the endpoint corresponding to the longest feeding/adaptation period was selected to preserve independence. The final database comprised 11 studies and 48 independent effect sizes.

Statistical analysis

The data analysis was conducted using a meta-analysis approach. Effect size calculations were performed using Hedge's g. Hedge's g is obtained by first defining Cohen's d. The calculations performed in this study are as follows:

$$d = \frac{Me - Mc}{S_{within}}$$

Where *Me* is the mean value of the treatment group and Mc is the mean value of the control group. S represents the standard deviation between the group means. d is the Cohen's d:

$$Swithin = \sqrt{\frac{(Ne-1)Se^2 + (Nc-1)Sc^2}{Ne + Nc - 2}}$$

Where Ne is the sample size of the treatment group, Nc is the sample size of the control group. Se is the standard deviation of the treatment group, and Sc is the standard deviation of the control group. Variance can be defined as:

$$V = \frac{N_e + N_c}{N_e + N_c} + \frac{d^2}{2(N_e + N_c)}$$

Table 1: Details of articles selected for the meta-analysis study.

No	Control Type	Experiment	Animal	Animal Sex	Ref.
1	Feed with Protein	Fasting	Llama	Female	Bakker *et al.* (1996)
2	Feed with protein	Feed without protein	Lamb	Female	Chen *et al.* (1990)
3	Feed with protein	Feed without protein	Sheep	Male	Chen *et al.* (1990)
4	Feed with protein	Fasting	Sheep and goat	Female	Fujihara *et al.* (2007)
5	Feed with protein	Feed without protein	Sheep	Male	Lestari *et al.* (2021)
6	Feed with protein	Feed without protein	Steer	Male	Verbic *et al.* (1990)
7	Feed with protein	Little feed protein	Sheep	Male	Hanim *et al.* (2019)
8	Feed with protein	Feed without protein	Lamb	Male	Silva *et al.* (2016)
9	Feed with protein	Feed without protein	Cow	Female	Henke *et al.* (2017)
10	Feed with protein	Feed without protein	Goat	Male	Harun *et al.* (2017)
11	Feed with protein	Feed without protein	Cow	Female	Castro-montoya *et al.* (2016)

A positive effect size is indicated by the observed parameter being larger than that of the control group, and vice versa. J is a correction factor for small sample sizes and is calculated as:

$$J = 1 - \frac{3}{4(Nc + Ne - 2) - 1}$$

The effect size value obtained from Hedge's g is calculated using the equation:

$$g = J \times d$$
$$Vg = J2 \times Vd$$
and $$SEg = \sqrt{V_g}$$

Borenstein *et al.* (2009). Data processing was carried out by importing Comma Separated Value (CSV) files from Microsoft Excel 2019 into the OpenMEE software for effect size and standard error calculations. A random-effects model was applied to account for the biological and methodological diversity across studies, assuming that true effect sizes varied among experiments. Effect sizes (Hedges' g) were computed in OpenMEE, while heterogeneity and publication-bias analyses were performed using JASP 0.16.2. To ensure comparability, fasting studies were analyzed separately from dietary treatments, recognising their distinct physiological mechanisms.

Heterogeneity was quantified using Cochran's Q and I^2 statistics, which indicated considerable variation (I^2> 98%) attributable to species and dietary differences. Consequently, the pooled estimates were interpreted as directional trends rather than absolute magnitudes, emphasizing consistency across subgroups. Sensitivity analyses, conducted by sequentially omitting individual studies, confirmed the stability of the results.

Publication bias, assessed by Egger's regression ($p < 0.001$) and funnel-plot asymmetry, suggested the presence of selective reporting. The application of the trim-and-fill method reduced the effect size slightly but did not alter its direction or significance. This potential bias is acknowledged as a limitation, and findings are interpreted cautiously within the biological framework of nitrogen metabolism in ruminants.

RESULTS AND DISCUSSION

In this meta-analysis, effect sizes were coded so that a positive Hedges' g indicates higher PD values under high-protein diets relative to the comparator (low-protein/protein-free), whereas a negative Hedges' g indicates lower PD values under high-protein diets. Therefore, the negative pooled estimates reported here should be interpreted as reduced PD excretion/levels in the high-protein group.

The results of the meta-analysis are summarised in Table 2. Overall, forest plots were generated to visualise the direction and precision of each study estimate and the pooled effect. The forest plot for allantoin is shown in Figure 2, uric acid in Figure 3, and xanthine+hypoxanthine in Figure 4.

For allantoin, the pooled effect size was strongly negative (SMD = −7.02; 95% CI: −10.85 to −3.20; $p < 0.001$), indicating that high-protein feeding was associated with lower allantoin compared with low-protein/protein-free diets (Table 2, Figure 2). This direction is important because allantoin is often considered a major end-product of purine catabolism and a commonly used indirect marker of microbial protein synthesis in ruminants. The magnitude of the pooled SMD is very large, and together with the extreme heterogeneity ($I^2 \approx 99.76\%$), it suggests that the estimate is highly influenced by between-study differences in diet formulation, animal type, sampling/analytical methods, and experimental contrasts rather than reflecting a uniform "high vs low protein" effect.

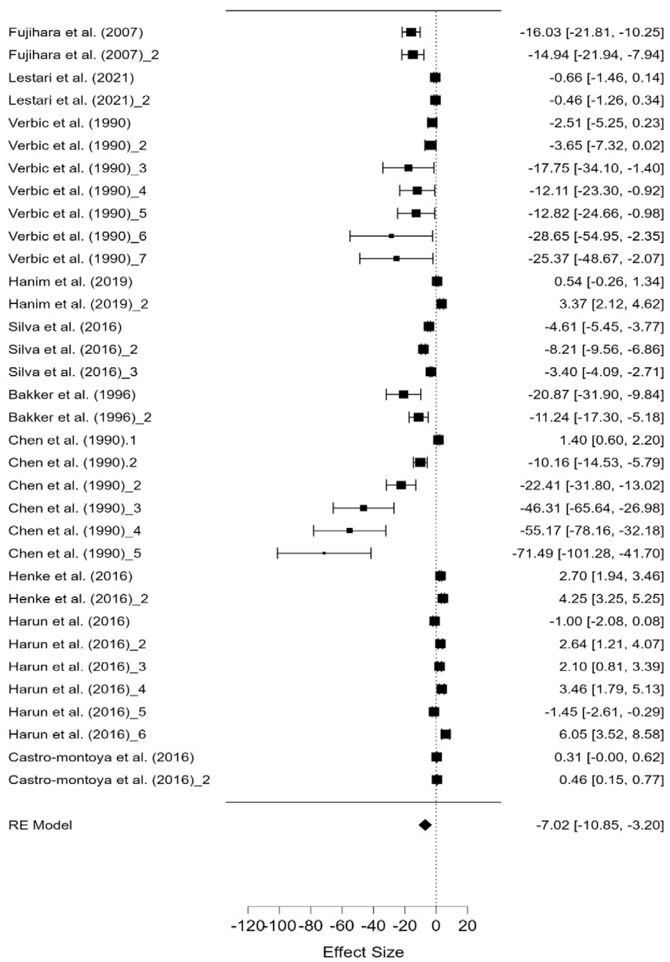

Figure 2: Forest plot of the effect of high-protein on allantion in ruminant livestock.

Biologically, the negative allantoin response under high-protein diets can be reconciled with rumen nitrogen dynamics when protein supply exceeds the capacity for microbial capture because fermentable energy and nitrogen release are not synchronised. Under such conditions, ammonia production may rise beyond microbialassimilation, reducing microbial growth efficiency and potentially lowering the microbial purine flow that ultimately contributes to urinary PD output (Verbic *et al*,. 1990; Zhou *et al*., 2017; Mahanani *et al*., 2021b; Pazla *et al*., 2025). This interpretation is consistent with the concept that microbial protein synthesis depends not only on crude protein supply but also on the synchrony of degradable nitrogen and fermentable carbohydrate availability in the rumen (Zhang *et al*., 2020).

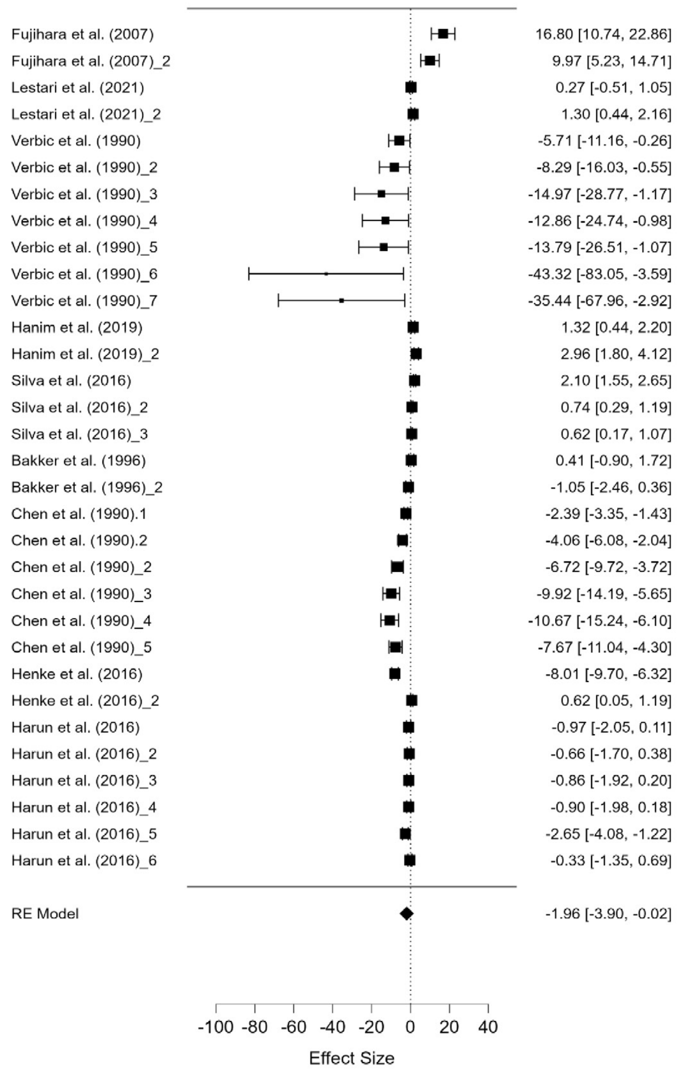

Figure 3: Forest plot of the effect of high-protein on urie acid levels livestock.

For uric acid, the pooled effect was also negative (SMD = −1.96; 95% CI: −3.90 to −0.02; p = 0.048), indicating a small but statistically significant reduction under high-protein feeding (Table 2, Figure 3). Compared with allantoin, uric acid showed greater variability in individual study directions, which is plausible given that uric acid may reflect not only microbial purine turnover but also post-ruminal purine metabolism and host tissue nucleic acid catabolism. Thus, uric acid may behave as a "more mixed" systemic signal than allantoin, potentially weakening the dietary contrast effect even when allantoin changes are pronounced.

Classically, higher nitrogen intake is expected to increase rumen microbial nitrogen production and, consequently, urinary PD excretion (Wang *et al*., 2017). Some individual studies also report higher purine outputs with protein-rich ingredients compared with energy-based diets (Mahanani *et al*., 2021b) and this aligns with the findings of Hu *et al*. (2025). However, the present meta-analysis indicates that in the evaluated dataset, higher protein supply was frequently associated with lower PD output. This apparent contradiction is biologically plausible if "high protein" in the included trials often coincided with (i) insufficient fermentable energy to capture ammonia into microbial protein, (ii) poor energy–nitrogen synchrony, and/or (iii) differences in degradability (RDP vs RUP) that shift nitrogen flow away from rumen microbial synthesis and toward post-ruminal digestion. Under such scenarios, PD excretion may decrease despite higher crude protein intake because microbial protein yield and purine outflow do not increase proportionally when nitrogen is oversupplied relative to energy (Ranilla and Carro, 2003; Ma, 2014; Verbic *et al*., 1990; Zhou *et al*., 2017).

Importantly, some contrasts in the dataset involve protein-free (and in some studies fasting) conditions, which represent nitrogen deprivation rather than a modest dietary adjustment. Such extreme comparators can amplify effect sizes and contribute to heterogeneity. Therefore, the pooled results should be interpreted as evidence that crude protein concentration alone is an insufficient descriptor, and that the response of PD is likely strongly modified by dietary context (energy availability, degradability, and adaptation period) rather than reflecting a universal "high protein reduces PD" law.

Additionally, low PD output could coincide with shifts in rumen fermentation, including VFA profiles, because microbial growth and fibre digestion depend on adequate nitrogen and branched-chain VFA supply. Diets differing in degradable true protein can alter iso-acid concentrations and, in turn, acetate patterns (Wang *et al*., 2017; Febrina *et al*., 2021a; Febrina *et al*., 2021b). Fibre-digesting bacteria require BCVFA for maximal activity (Bryant, 1973; Wang *et al*., 2019), and iso-acid supplementation can stimulate fibre digestibility and influence acetate concentration (Soltani *et al*., 2017). Collectively, these points reinforce that diet formulation should target a balance between rumen-degradable protein and degradable energy rather than maximising crude protein.

Table 2: Descriptive statistics of database.

Parameters	n	SMD/d	Lower	Upper	p-SMD	I^2(%)	p-Egger
Allantoin	11	-7,022	-10,847	-3,198	<0,001	99,76	<0,001
Uric acid	10	-1,959	-3,900	-0,018	0,048	98,85	<0,001
Xanthine + Hypoxanthine	8	-0,874	-2,569	0,820	0,312	98,19	0,026

n= number of articles used; SMD/d= Standardized Mean Difference; Lower= Lower Limits of the 95% Confidence Interval; Upper= Upper Limits of the 95% Confidence Interval; p-SMD= p-value Standardized Mean Difference; I2= Heterogeneity; p-Egger= p-value Egger's test.

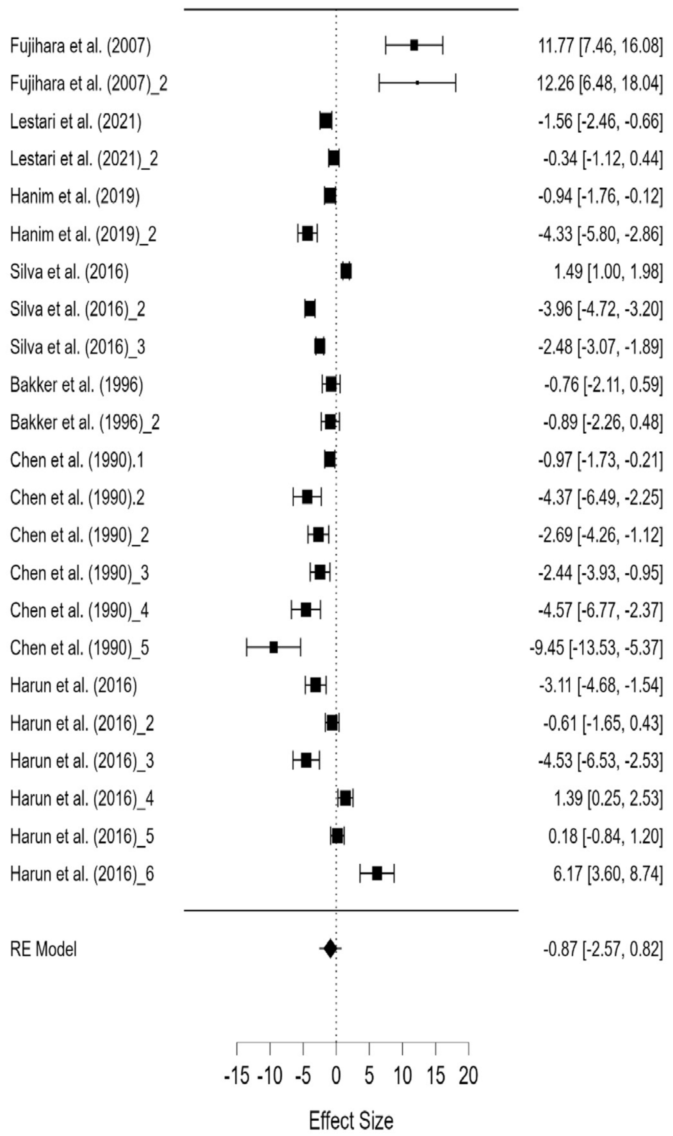

Figure 4: Forest plot of the effect of high-protein feed on xanthine hypoxanthine levels in ruminant livestock.

For xanthine+hypoxanthine, the pooled estimate was negative but non-significant (SMD = −0.87; 95% CI: −2.57 to 0.82; p = 0.312; $I^2 \approx 98.2\%$) (Table 2, Figure 4). Individual studies varied considerably, with some reporting increases (Fujihara *et al.*, 2007; Harun *et al.*, 2017) and others decreases (X. B. Chen *et al.*, 1990; Silva *et al.*, 2016). Because xanthine and hypoxanthine are upstream intermediates in purine catabolism, their concentrations can be shaped by multiple processes (microbial turnover, salvage pathways, and host enzymatic conversion). The lack of a consistent pooled effect suggests that high-protein feeding does not uniformly affect early purine-catabolism intermediates, even when downstream metabolites (allantoin and uric acid) show reductions. This may indicate buffering or pathway-level variability across diets and experimental contexts (Hu *et al.*, 2025).

The funnel plot asymmetry and significant Egger's test ($p < 0.05$) indicate risk of small-study effects/publication bias (Table 2, Figure 5). However, it is not correct to state that publication bias is "minimised" by applying a random-effects model. Random-effects models address between-study heterogeneity, but they do not correct selective reporting or selective publication. This is particularly relevant here because with a small number of studies per outcome (≈8–11) and extreme heterogeneity, funnel-plot asymmetry and Egger's regression can also reflect genuine heterogeneity, metric choice, or chance rather than publication bias alone (Nakagawa *et al.*, 2022; Afonso *et al.*, 2024).

From an environmental perspective, if high-protein feeding does not translate into proportional microbial capture and productive use, excess nitrogen is more likely to be excreted (especially in urine), increasing the potential for ammonia and other nitrogen losses. This manuscript's inference is therefore mainly qualitative (directional) because the meta-analysis pooled PD outcomes rather than direct nitrogen excretion metrics. Nevertheless, evidence from dairy housing and emission studies shows that reducing crude protein intake can reduce urinary nitrogen and ammonia emissions, supporting the plausibility of increased nitrogen losses under protein oversupply (Schrade *et al.*, 2023). The general point that only a fraction of nutrients are retained and the remainder excreted also supports this interpretation (Teenstra *et al.*, 2015).

More robust sensitivity analyses for selective publication have been proposed in the broader meta-analysis literature (Mathur, 2024), and such approaches may be considered in future work to evaluate how strongly selective publication would need to operate to overturn the main conclusions.

Finally, the I^2 values approaching 99% indicate that the "high vs low protein" contrast is likely too coarse to explain the variability across studies. The most defensible

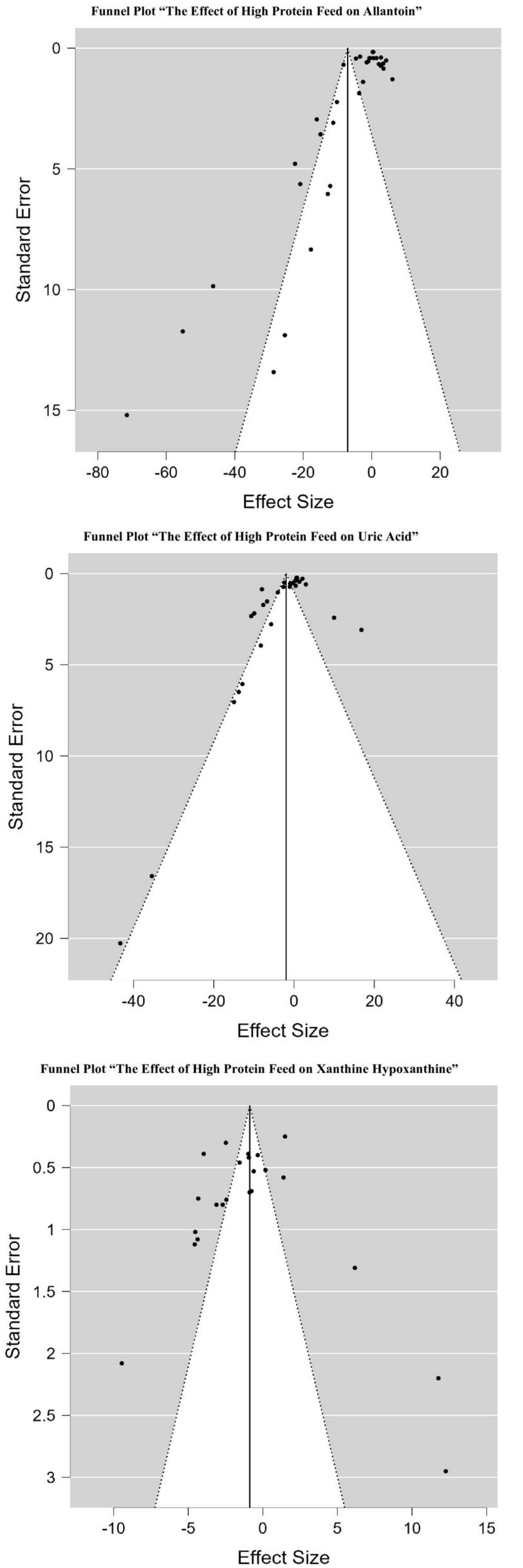

Figure 5: Funnel plot off the effect of high-protein feed on purine derivatives in ruminant livestocks.

interpretation is that the pooled estimates represent an average across highly diverse conditions and should be treated as directional. Future syntheses should prioritise moderator analyses (species, protein source and degradability, fermentable energy supply, adaptation period, measurement matrices) and clearer comparator definitions to reduce conceptual and statistical heterogeneity.

CONCLUSION

It can be concluded that high-protein diets were often associated with lower urinary purine derivative excretion. Therefore, the relationship between dietary protein level and purine derivatives appears context-dependent, likely influenced by protein–energy synchrony and diet composition, and warrants further controlled studies with better reporting of key dietary modifiers (e.g., RDP/RUP and fermentable carbohydrate indices).

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NOVELTY STATEMENT

This study is the first meta-analysis examining the relationship between dietary protein level and urinary purine derivative excretion in ruminants. Contrary to the common assumption, the pooled evidence shows that high-protein diets were often associated with lower allantoin and uric acid excretion, highlighting a context-dependent paradox shaped by protein–energy synchrony and diet composition.

AUTHORS' CONTRIBUTION

DF, NQ: Format analysis; DF, RPH: Visualization; DF, NQ, JAP, SS, MJA, ERAR: Writing-review and editing; DF: Conceptualization; DF, SS: Supervision; AJ, RPH: Data curation; DF: Methodology; DF, NQ: Writing-original draft; DF: Project-administration; SS: Resources; RPH, SS: Software; AJ: Validation.

Generative AI and AI-assisted technology statement

The authors used generative AI tools only for language refinement, and they take full responsibility for the accuracy and integrity of the manuscript's scientific content.

Conflict of interest

All authors declare that there is no conflict of interest.

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