



Research article

The molecular signature of umami palatability in dogs based on amino acid interactions with canine taste receptors

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Arun HS Kumar

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Canine feeding behaviour is strongly influenced by taste perception; however, the molecular determinants of palatability, particularly those associated with umami taste, remain insufficiently characterized. Dogs typically consume food rapidly with minimal mastication and rely on a relatively small number of taste buds to detect sour, bitter, salty, sweet, and umami flavours. Amino acids play a central role in canine taste perception, especially in diets rich in animal proteins. This study aimed to identify the amino acids that most effectively stimulate umami perception in dogs using a receptor–ligand docking approach. Twenty-seven canine-specific taste receptors were identified from the UniProt database, including three umami, two sweet, five uncharacterized, and seventeen bitter receptors. All twenty naturally occurring amino acids were docked against these receptors using the CB-Dock tool, and their binding affinities were systematically analyzed. Heat maps of binding energies indicated that tyrosine, tryptophan, arginine, histidine, phenylalanine, glutamine, glutamic acid, and lysine exhibited the strongest interactions with umami and sweet receptors, while bitter and uncharacterized receptors showed weaker affinities. Binding energy ratio analyses further demonstrated that amino acids preferentially stimulated umami and sweet receptors, with lysine, histidine, glutamine, glutamic acid, and arginine identified as key co-stimulators. Functional enrichment analyses revealed that these receptors are members of Class C/3 G protein-coupled receptors (GPCRs), with membrane-bound sweet receptor complexes and strong associations with the sensory perception of umami, sweet, and bitter tastes. These findings provide a molecular basis for enhancing palatability in canine diets and have practical implications for the formulation of dry dog food and the development of oral veterinary medicines. The results underscore the importance of specific amino acids, potentially in combination with salts, in modulating taste responses and improving food acceptance in dogs.

Keywords: Amino acids, Canine taste receptors, Gustation, GPCR, Molecular docking, Palatability, Pet nutrition, Umami

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Introduction

Domestic dogs display characteristic feeding behaviour, such as rapid food consumption with limited mastication or savouring (Bradshaw, 2006; Schipper et al., 2008). This pattern is primarily attributed to their reduced gustatory capacity, as dogs possess significantly fewer taste buds than humans (Breslin and Spector, 2008; Koppel et al., 2015). Despite this limitation, dogs can detect the five primary taste

modalities, sour, bitter, salty, sweet, and umami, by activating specific chemoreceptors (Bradshaw, 2006; Watson et al., 2023). Umami perception is particularly important because it is associated with the detection of amino acids and nucleotides, which are abundant in animal tissues and play a central role in canine dietary preferences.

Food selection in dogs is determined by both

nutritional adequacy and immediate palatability. Palatability arises from the combined effects of sensory cues, including taste, aroma, texture, size, appearance, temperature, and consistency (Alegria-Morán et al., 2019; Holland, 2019; Morgan et al., 2022). Additionally, genetic factors and early-life experiences influence canine food preferences, complicating the optimization of commercial diets (Alegria-Morán et al., 2019). Dogs demonstrate heightened sensitivity to amino acids, organic acids, and nucleotides, indicating that these molecules play a significant role in palatability-driven feeding behaviour (Oberbauer and Larsen, 2021; Watson et al., 2023). Managing palatability in dry pet foods is particularly challenging, as these diets typically include carbohydrate sources (such as cereals), protein sources (including fresh, frozen, or rendered animal meals), by-products, and lipid sources of animal or plant origin (Koppel et al., 2015). The characteristics of these ingredients, along with their processing and incorporation methods (such as blending, concentration, or surface coating), are critical determinants of overall product appeal.

Commercially successful dry dog foods utilize a diverse range of protein ingredients. Animal-derived proteins such as chicken, turkey, salmon, fish, and mixed poultry are commonly included, while beef, lamb, venison, duck, and rabbit are also frequently used to diversify flavour profiles and address consumer preferences (Dust et al., 2005; Raghavan et al., 2006; Montegiove et al., 2021; Sieja et al., 2023). In recent years, novel and nontraditional protein sources have been introduced, particularly in formulations for dogs with sensitivities or those requiring alternative protein options (Dust et al., 2005; Montegiove et al., 2021; Klinmalai et al., 2025). Protein selection ensures the provision of essential amino acids and directly influences palatability, as different animal tissues impart unique sensory characteristics. Beyond protein type, the molecular composition of diets is a critical factor in shaping canine taste perception (Koppel et al., 2015). Specific amino acids, including L-phenylalanine, L-tyrosine, L-tryptophan, L-methionine, L-arginine, L-leucine, and L-serine, are particularly important for enhancing flavour responses and improving palatability (Samant et al., 2021; Watson et al., 2023). Additionally, salts such as sodium,

potassium, and calcium can synergistically enhance the taste responses elicited by these amino acids, thereby increasing overall product appeal (Kumazawa et al., 1991; Ugawa and Kurihara, 1994). Incorporating these factors into dry food formulations is essential to achieve a balance between nutritional adequacy and sensory acceptance, a central challenge in canine diet design.

Although commercial canine diets incorporate a variety of meat sources to enhance flavour and nutritional value, the molecular mechanisms underlying palatability remain incompletely understood (Montegiove et al., 2021; Sieja et al., 2023). Current formulations frequently rely on empirical ingredient selection rather than on systematic evaluation of specific amino acid interactions with canine taste receptors that mediate umami perception. While amino acids are central to flavour enhancement, a receptor-ligand-based framework for identifying which amino acids most effectively stimulate umami taste in dogs has not yet been established. Establishing such a framework would provide valuable insights into the molecular determinants of taste perception and support the rational design of canine diets with optimized palatability. Given the importance of amino acid perception in canine feeding, this study systematically evaluates the interactions between all 20 naturally occurring amino acids and the full repertoire of known canine taste receptors using molecular docking. This methodology establishes a mechanistic basis for understanding umami-driven palatability in dogs and informs the targeted use of palatability factors in dry dog foods to improve acceptance.

Materials and methods

All dog-specific taste receptors reported in the literature and available in UniProt databases were included in this study. The complete repertoire of canine taste receptors, encompassing those associated with sweet, sour, salty, bitter, and umami perception, was compiled. The receptor genes were then subjected to protein-protein interaction (PPI) network analysis using STRING (Search Tool for the Retrieval of Interacting Genes/Proteins, version 12.0). STRING was chosen for its ability to predict both direct (physical) and indirect (functional) associations by integrating data from curated databases, experimental results, co-expression,

and text mining. To ensure high confidence, interaction scores were filtered using a minimum confidence threshold of 0.7, and only experimentally validated or strongly predicted interactions were retained for further analysis. The resulting PPI networks were visualized and topologically analyzed to identify hub nodes, clusters, and modules that may represent key signaling pathways involved in taste perception. Network statistics, including degree centrality, betweenness centrality, and clustering coefficients, were calculated to assess the relative importance of specific receptors within the network.

Gene ontology (GO) enrichment analysis was performed to derive biological insights from the identified receptor interaction networks. GO functional annotation tools integrated into STRING (version 12.0) were used for cross-validation. Enrichment was evaluated across three GO categories: biological processes, molecular functions, and cellular components. The statistical significance of enriched GO terms was determined using the Benjamini–Hochberg false discovery rate (FDR) correction, with p -values <0.05 considered significant. This integrated network analysis and GO enrichment approach provided a systems-level understanding of the functional landscape of canine taste receptors and established the foundation for subsequent receptor–ligand docking studies aimed at identifying amino acids that optimally enhance umami palatability in dogs.

A total of 27 canine-specific taste receptors were identified and retrieved from the UniProt database. These receptors included members of the bitter (TAS2R), sweet/umami (TAS1R2/TAS1R3,1), and other chemosensory receptor families known to be functionally relevant in dogs. Protein sequences were obtained in FASTA format. When experimental crystal structures of full-length proteins were unavailable, three-dimensional (3D) structures were modeled as previously reported (Kumar, 2024; Rao and Kumar, 2025). Homology modeling was performed using SWISS-MODEL, and the resulting models were validated using structural quality assessment metrics, including GMQE, QMEAN, and Ramachandran plot statistics. Where available, experimentally resolved structures from the Protein Data Bank (PDB) were used directly.

Of the 27 receptors identified, three were classified as umami-associated, two as sweet-associated, five as orphan or unknown receptors with uncharacterized specificity, and the remaining 17 as bitter taste receptors. This distribution underscores the evolutionary emphasis on bitter taste perception in dogs, which likely serves as a protective mechanism against ingestion of harmful compounds, while maintaining a smaller but functionally important set of receptors for detecting amino acid and nucleotide-based flavors such as umami.

All 20 naturally occurring amino acids were evaluated as ligands in the docking studies. The three-dimensional structures of the amino acids were retrieved in SDF format from the PubChem database, converted to PDB format, and energy-minimized in Chimera (version 1.19) to ensure geometric stability prior to docking (Kumar, 2022; Kumar, 2024; Rao and Kumar, 2025). Molecular docking was conducted using the CB-Dock tool, an automated Web server for cavity-guided, blind docking. Each receptor underwent cavity detection to identify potential ligand-binding sites, followed by docking simulations for all 20 amino acids against each receptor. CB-Dock uses AutoDock Vina as its docking engine, which computes binding affinities from predicted free binding energies (kcal/mol) (Kumar, 2022; Kumar, 2024; Rao and Kumar, 2025). For each receptor–ligand pair, the top-ranked docking poses were selected according to binding energy scores. The details of the docking parameters used are summarised in Supplementary File 1.

Docking results were systematically compiled to identify amino acids with the strongest predicted binding affinities across the canine taste receptor repertoire. Emphasis was placed on receptors associated with umami taste (such as TAS1R1 and TAS1R3), while comparisons were also made across all receptor families to assess broader selectivity trends. The binding interactions of the top amino acids were visualized and analyzed in Chimera (version 1.19) to examine hydrogen bonding, hydrophobic interactions, and other non-covalent interactions that stabilize the receptor–ligand complexes (Kumar, 2024; Rao and Kumar, 2025). Docking simulations produced binding energy values (kcal/mol) for each receptor–amino acid pair, reflecting the predicted affinity of each ligand for the respective canine taste receptor. These values were compiled into a receptor–ligand interaction

matrix, with columns representing the 27 taste receptors and rows representing the 20 naturally occurring amino acids. This dataset enabled comparative evaluation of binding affinities across the receptor repertoire. The average binding energy values or ratios of binding energy of each amino acid to all the taste receptors or the major taste receptor category (umami, sweet, bitter, and unknown) are reported as Mean±SD.

To facilitate interpretation, binding energy data were visualized as heat maps. Heat maps were constructed in the R statistical environment (version 4.4.2) using the “pheatmap” package, enabling hierarchical clustering of both receptors and ligands based on their affinity profiles (Kumar, 2024; Rao and Kumar, 2025). Color gradients were applied, with lower (more negative, shown in green) binding energy values indicating stronger affinities, thereby visually highlighting amino acids with a preference for specific receptors. Clustering analysis identified groups of amino acids with similar binding patterns and receptor subgroups with overlapping affinity profiles. This heat map approach provided a comparative framework to assess the relative affinities of amino acids across all identified canine taste receptors and supported the identification of key ligand–receptor interactions potentially associated with umami taste enhancement.

To further examine the selective preference of specific amino acids for umami taste receptors, binding energy ratio analyses were conducted. For each amino acid, the receptor with the highest binding affinity (lowest binding energy) was identified and used as the normalization reference. Binding energy values for the same amino acid across all other receptors were then expressed as ratios relative to this reference value. This normalization enabled assessment of amino acid selectivity by accounting for inherent differences in docking scores. The normalized binding energy ratios (reported as Mean ± SD) were grouped by receptor type: umami, sweet, bitter, and unknown. For each category, the average ratio was calculated, allowing comparison of how strongly individual amino acids were predicted to interact with umami receptors relative to other receptor classes. This analysis provided a quantitative framework for identifying amino acids most likely to contribute to strong umami-driven taste perception in dogs.

As an additional assessment, pairwise

binding energy ratios were calculated between receptor categories to evaluate the dominant taste sensation that each amino acid might elicit. The following category pairs were examined: umami/sweet, umami/bitter, umami/other, sweet/bitter, sweet/other, and bitter/other, where “other” refers to the group of five unknown receptors. These ratio comparisons highlighted the relative strength of amino acid interactions across different taste modalities, providing insight into whether a given amino acid preferentially activates umami-associated receptors compared to other taste receptor classes. This ratio-based approach enabled a more nuanced evaluation of receptor–ligand specificity beyond raw binding energy values and supported the identification of amino acids most likely to enhance umami palatability in canine diets. Details of the taste receptors (gene, type, UniProt ID, similarity of the homology-modeled structure) are listed in Supplementary File 2.

Results

Network analysis of canine taste receptors revealed a highly interconnected protein-protein interaction (PPI) network. The constructed network comprised 15 nodes and 83 edges, with an average node degree of 11.1, indicating that each receptor was connected to multiple partners within the group. The average local clustering coefficient was 0.899, suggesting a strong tendency for receptors to form tightly clustered interaction neighborhoods rather than existing as isolated units. The analysis further showed an expected number of edges of 0, while the observed number of edges was substantially higher. The PPI enrichment p-value was $< 1.0e-16$, confirming that the observed interactions were highly significant and not attributable to random chance. This enrichment indicates that canine taste receptor proteins share functional and biological relationships, forming a cohesive interaction network. These findings suggest that canine taste receptors participate in a biologically meaningful, interconnected system that potentially underlies coordinated roles in taste perception and related signaling pathways. A dense subnetwork within the TAS1R family indicates strong integration of the sweet and umami pathways, reflecting attraction to both sugars and protein-rich foods in dogs. In contrast, the bitter receptor cluster is positioned more peripherally, consistent with a carnivorous dietary bias and a diminished need for broad

detection of plant-derived toxins. The network architecture illustrates an evolutionary balance in canine taste perception, preserving attraction to calorie- and protein-dense foods.

Tissue enrichment analysis indicated that the identified canine taste receptors were exclusively expressed in taste buds, with the majority classified as type 2 taste receptors. Receptor Classification and Tissue Mapping (RCTM) analysis demonstrated high enrichment for sensory perception of sweet, umami (glutamate), and bitter taste modalities, consistent with their classification as Class C/3 (metabotropic glutamate/pheromone receptors) with G α (i) signaling pathways. Further receptor annotation confirmed that all identified canine taste receptors belong to the Class C/3 GPCR family, group 3. Functional enrichment data indicated that both general taste receptor activity and bitter taste receptor activity were equally prominent, highlighting the evolutionary role of bitter perception in dogs alongside nutrient-driven modalities. Compartment enrichment analysis further indicated that the receptor associates with membrane-bound sweet taste receptor complexes, suggesting a structural role in receptor clustering and signaling efficiency.

Docking analysis of 20 naturally occurring amino acids against 27 canine taste receptors revealed several key trends. Tyrosine, tryptophan, arginine, and phenylalanine consistently exhibited the highest binding affinities across most taste receptors, underscoring their broad role in canine taste perception. By receptor type, tyrosine, tryptophan, arginine, histidine, phenylalanine, glutamine, glutamic acid, and aspartic acid demonstrated strong binding specifically to umami-associated receptors. In contrast, tyrosine, tryptophan, phenylalanine, isoleucine, leucine, lysine, histidine, glutamine, glutamic acid, and arginine displayed high affinity toward sweet receptors. For bitter and unclassified (orphan) receptors, tyrosine, tryptophan, and phenylalanine exhibited the strongest affinities. These results align with prior reports identifying tyrosine, tryptophan, serine, methionine, leucine, and arginine as major stimulators of umami taste receptors, thereby validating the docking outcomes. The affinity values of all amino acids to all the receptor categories are listed in Supplementary File 2.

To further delineate amino acid selectivity, binding energy ratios were calculated by normalizing each amino acid's receptor affinities against its strongest binding interaction. This analysis revealed that both sweet and umami receptor categories were equally and strongly stimulated by amino acids, with significantly higher ratios than those observed for bitter and unknown receptor types. The average binding energy across receptor categories supported this pattern, with lysine, histidine, glutamine, glutamic acid, and arginine emerging as major co-stimulators of both sweet and umami receptors. Pairwise ratio comparisons between receptor categories provided additional insight into the relative dominance of taste responses. The umami/bitter, umami/other, sweet/bitter, and sweet/other groups exhibited significantly higher ratios, indicating that amino acids preferentially stimulated sweet and umami receptors over bitter and unknown receptors. The umami/sweet ratio was close to 1.0, suggesting equal stimulation of both receptor types by a broad range of amino acids. The unknown receptor group consistently exhibited the weakest binding affinities and the lowest ratio values, reinforcing its limited role in amino acid-mediated taste perception. This relative affinity framework identifies lysine, histidine, glutamine, and glutamic acid as the most potent and selective co-stimulators of umami- and sweet-receptor classes in dogs.

Discussion

This study establishes a comprehensive receptor-ligand-based framework for investigating the molecular basis of umami and sweet taste perception in dogs by molecular docking of 20 naturally occurring amino acids against 27 canine-specific taste receptors. The observations are exclusively based on *in silico* evaluations and lack *in vivo* validation; therefore, the results should be interpreted in light of the recognized limitations of docking studies involving G protein-coupled receptors (GPCRs) (Derval, 2022; Doyle et al., 2023). The findings indicate that amino acids such as lysine, histidine, glutamine, and glutamic acid play prominent roles in selectively stimulating umami and sweet receptors, while exhibiting comparatively weaker affinities toward bitter and unknown receptor classes. These results highlight the dual importance of umami and sweet perception in shaping canine food preferences and provide a molecular foundation for improving palatability in commercial diets.

The implications extend to canine nutrition and veterinary medicine, as palatability is a key determinant of acceptance for commercially prepared foods (Davies et al., 2019; Raditic, 2021). As the pet food industry increasingly adopts sustainable protein sources, including alternative and non-animal proteins, challenges related to palatability are expected to intensify (Mylan et al., 2023; Gil et al., 2024). The identification of amino acids that selectively stimulate sweet and umami receptors provides a molecular basis for enhancing acceptance of such formulations. Additionally, dogs' strong aversion to bitter tastes presents a challenge for the oral delivery of veterinary medicines (Thombre, 2004; Song et al., 2016). Elucidating the receptor-level mechanisms of taste perception may inform the design of formulations that mask bitterness while leveraging amino acid-mediated stimulation of sweet and umami receptors to improve compliance in oral drug administration.

Network and enrichment analyses provide new insights into the organization and functional relevance of canine taste receptors. The highly interconnected PPI network observed in this study, with significant enrichment well beyond random expectations, indicates that taste receptors in dogs operate as a coordinated system rather than isolated sensory units. This observation aligns with previous findings in humans and rodents, where taste receptors have been shown to interact within broader signaling frameworks to fine-tune perception (Derval, 2022; Doyle et al., 2023). The dense subnetwork formed by TAS1R family members suggests strong functional integration of sweet and umami pathways. This may reflect the dual importance of sugars and amino acid-rich foods in canine diets, consistent with evidence that dogs are particularly sensitive to amino acids, nucleotides, and other compounds abundant in animal tissues (Koppel et al., 2015). The peripheral placement of bitter receptors in the network supports the hypothesis of the carnivorous origins of dogs, in which the selective pressure for broad detection of plant-derived toxins is reduced compared to that in omnivores. This positioning suggests that bitter receptors, while still functionally relevant, play a secondary role relative to umami and sweet perception. The enrichment analyses further support this interpretation by showing exclusive

expression of receptors in taste buds, high representation of Class C/3 GPCRs, and strong associations with sweet, umami, and bitter modalities. The equal prominence of general and bitter taste receptor activities echoes prior work highlighting the evolutionary conservation of bitter perception as a safeguard, even in carnivorous species (Glendinning, 1994; Jiang et al., 2012; Wooding et al., 2021). The evolution of canine taste receptors as a tightly integrated network that prioritizes attraction to nutrient-rich foods while maintaining the ability to detect aversive compounds offers critical insights into the development of highly palatable diets.

The observed strong functional integration between the sweet and umami pathways in the network analysis aligns with the finding that both receptor classes were equally stimulated by amino acids. This relationship also correlates with dogs' physiological feeding behavior (Bradshaw, 2006; Part et al., 2014). Unlike humans, dogs do not spend significant time mitigating or savoring; instead, they consume food rapidly and in a gluttonous manner (Gerstner et al., 2010; Arhant et al., 2021). This behavioral tendency is accompanied by fewer taste buds than in humans (Koppel et al., 2015). Despite this limitation, dogs can detect all five primary taste modalities, and the strong stimulation of sweet and umami receptors may compensate for their limited gustatory capacity, ensuring efficient detection of nutrient-rich foods (Singletary and Lazarowski, 2021). Given that amino acids, organic acids, and nucleotides are abundant in animal tissues, heightened canine sensitivity to these compounds is consistent with an evolutionary adaptation toward a carnivorous-leaning diet (Oberbauer and Larsen, 2021). The implications of these findings extend directly to the formulation of commercial dry dog food. Palatability in dogs is determined by a combination of factors, including aroma, texture, size, appearance, temperature, and consistency, as well as taste (Koppel et al., 2015). Amino acids that strongly stimulate umami and sweet receptors, particularly lysine, histidine, glutamine, and glutamic acid, could serve as key molecular drivers of enhanced food acceptance. Several amino acids (tyrosine, tryptophan, arginine, and phenylalanine) have been consistently identified as key contributors to palatability in canine diets (Oberbauer and Larsen, 2021; Watson et al., 2023).

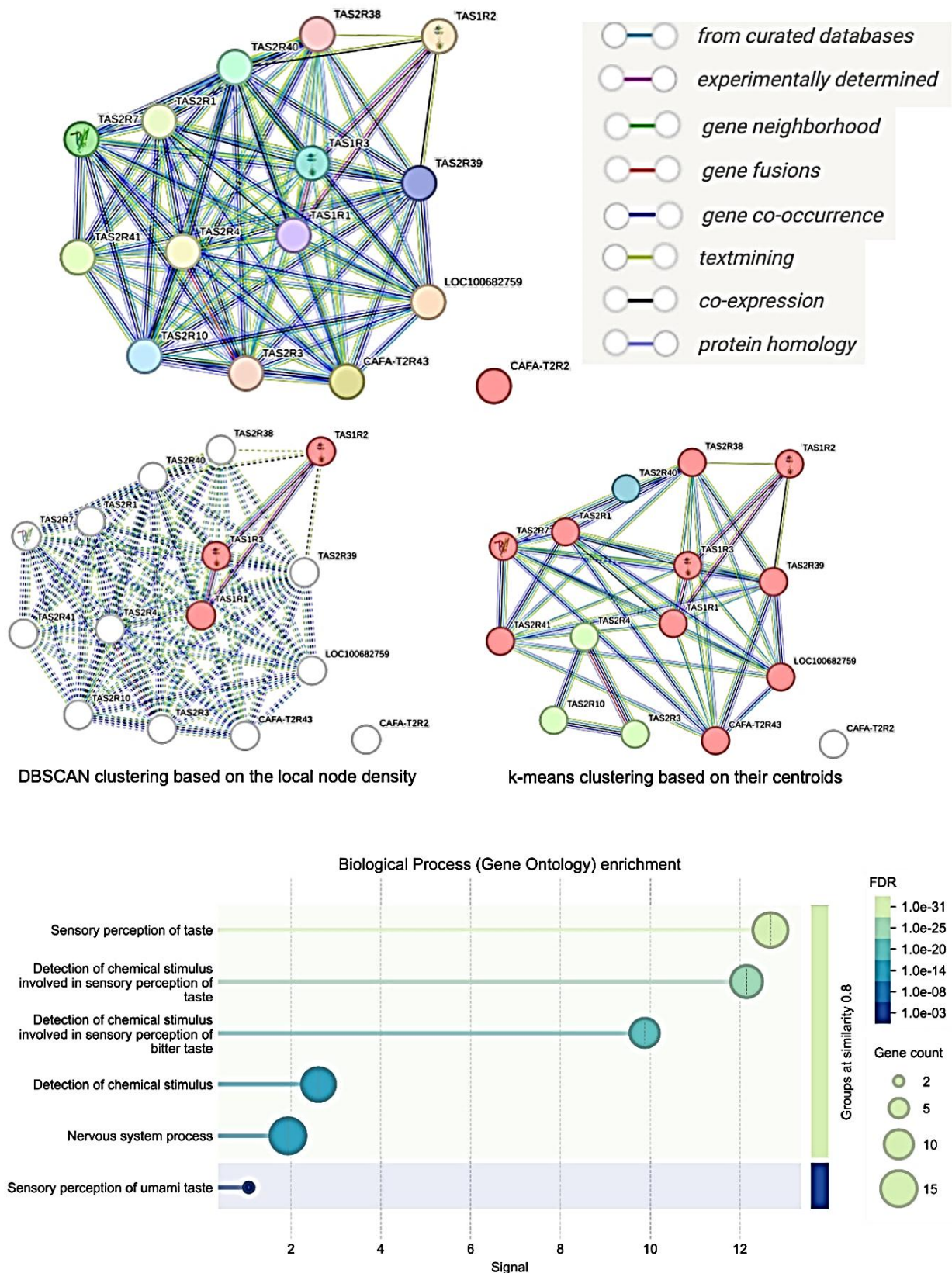


Figure 1: Network analysis and functional enrichment of canine taste receptors. Each node represents an individual taste receptor encoded by a single, protein-coding gene locus with edges indicating predicted or experimentally validated protein–protein interactions. Canine taste receptors were further organized based on local node density and centroid-based clustering to highlight functional subnetwork relationships. The bubble plot represents Gene Ontology (GO) enrichment analysis of the network, displaying significantly enriched biological processes. False discovery rate (FDR).

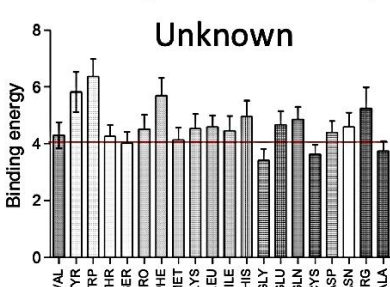
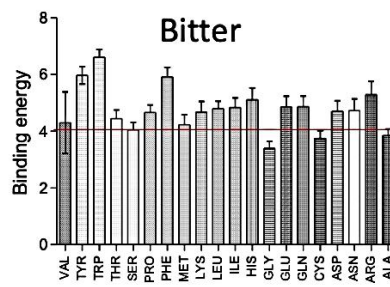
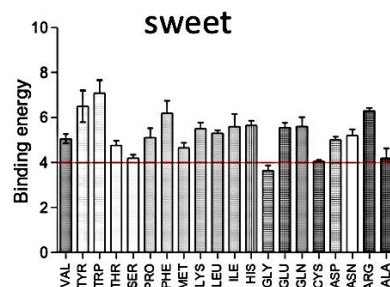
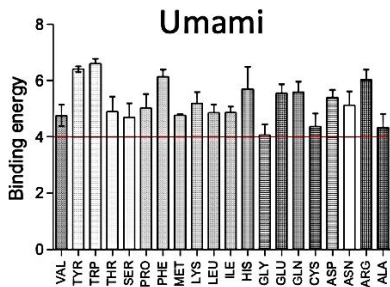
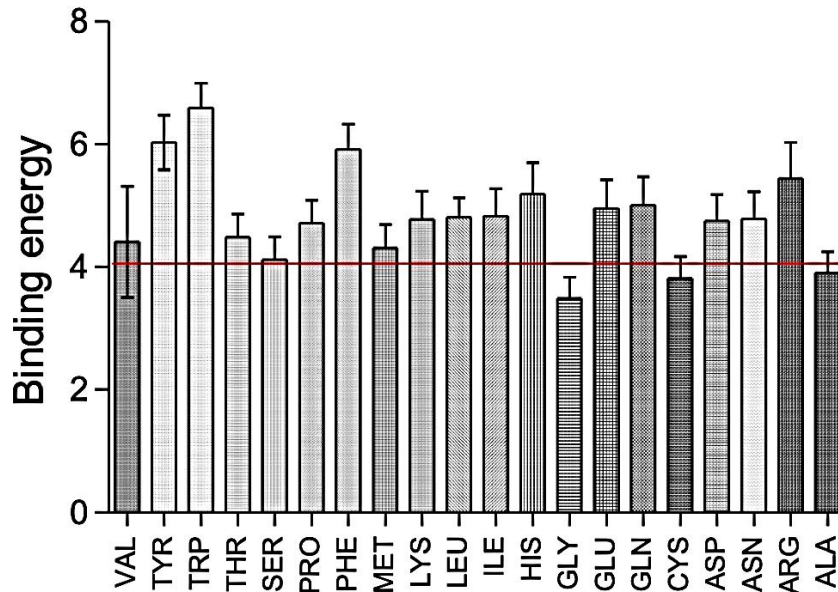
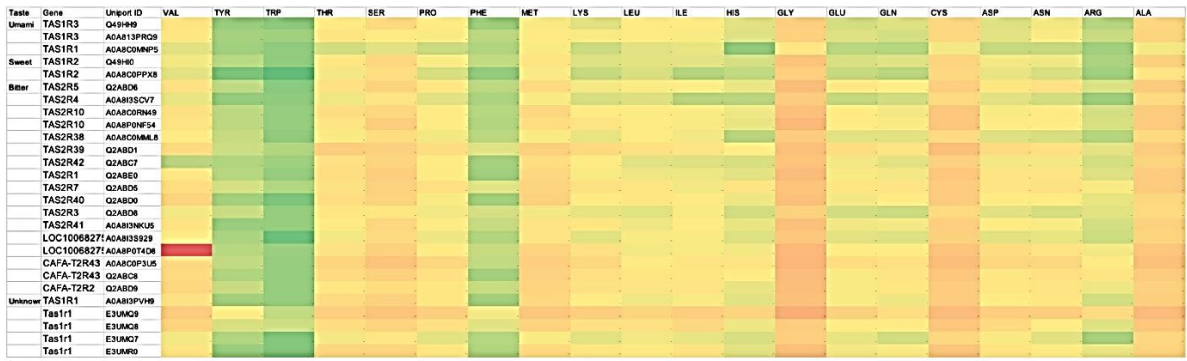


Figure 2: Heatmap and comparative binding energy profiles of amino acids across canine taste receptor classes. The heatmap illustrates the binding energy values of all 20 naturally occurring amino acids docked against the full set of canine taste receptors, highlighting differential affinities across receptor types. Each cell represents the predicted binding energy (kcal/mol), where lower values (green) indicate stronger ligand–receptor interactions. The bar graphs display the average binding energy (mean \pm SD) of each amino acid with all canine taste receptors combined, as well as separately for umami, sweet, bitter, and unknown receptor categories.

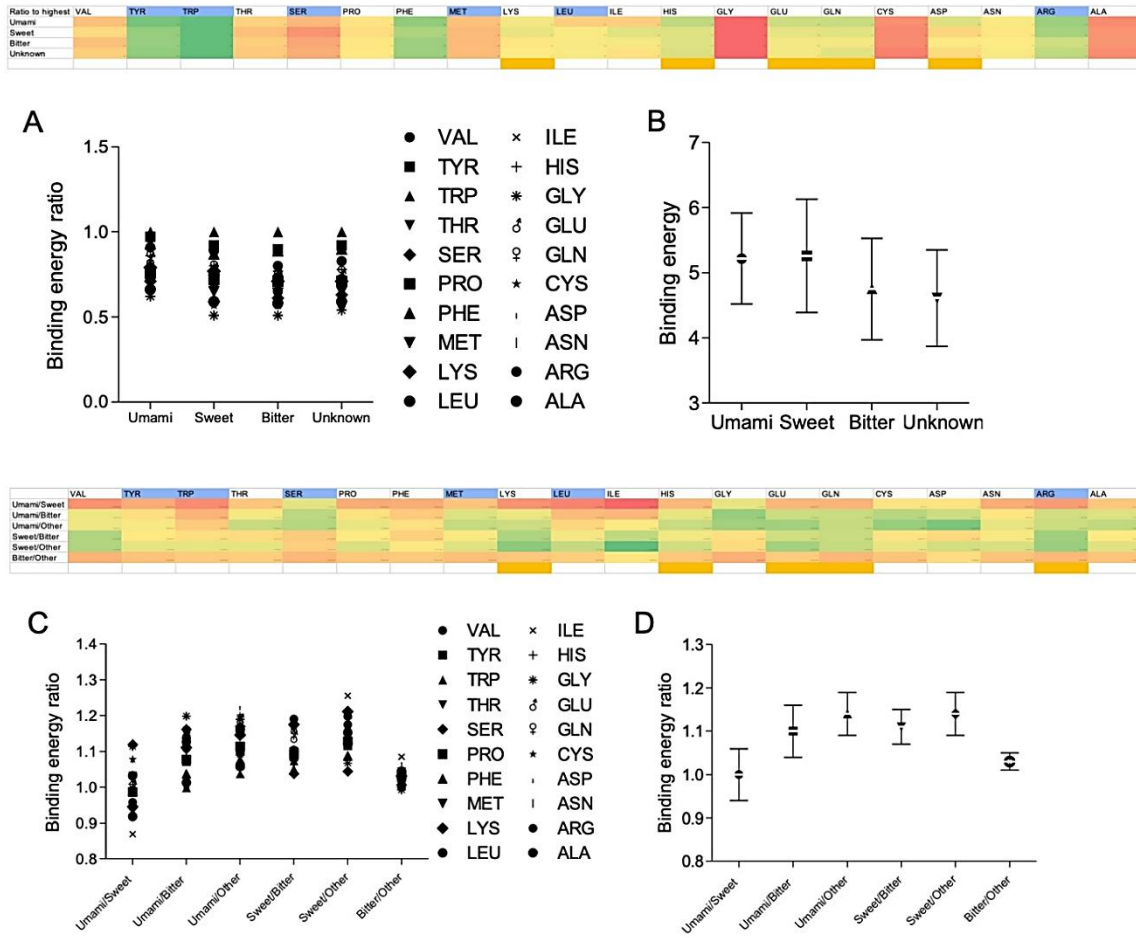


Figure 3: Comparative analysis of amino acid binding energy ratios across canine taste receptor categories. The heatmap illustrates the binding energy ratios of 20 naturally occurring amino acids with the four major classes of canine taste receptors: umami, sweet, bitter, and unknown. Corresponding bar graphs display (A) the mean binding energy ratios and (B) the average binding energy values (kcal/mol) of each amino acid across receptor categories, presented as mean \pm SD. The lower heatmap depicts the binding energy ratios of the same 20 amino acids across pairwise receptor comparisons (umami/sweet, umami/bitter, umami/unknown, sweet/bitter, sweet/unknown, and bitter/unknown). Bar graphs show (C) the mean binding energy ratios and (D) the average of these ratios (mean \pm SD) for each amino acid pairwise comparison.

The importance of these amino acids has been linked to their strong sensory impact and prevalence in animal-derived protein sources, which dominate most commercial formulations. While these amino acids demonstrate strong binding potential, their interactions are not restricted to a single taste modality. Tyrosine, tryptophan, arginine, and phenylalanine exhibit comparable affinities across sweet, umami, bitter, and unknown receptor classes. This broad responsiveness suggests that these amino acids may function as general taste modulators, contributing to multiple sensory pathways rather than selectively driving umami or sweet perception. However, their non-selective affinity toward bitter receptors raises an important consideration: foods rich in tyrosine,

tryptophan, arginine, and phenylalanine may not always translate into highly palatable diets for dogs. While these amino acids can stimulate nutrient-positive tastes such as sweet and umami, their concurrent activation of bitter receptors may introduce aversive signals that diminish overall acceptance. Bitter taste perception in dogs, as in many mammals, is often associated with the detection of potentially harmful or toxic compounds (Wooding et al., 2021; Itoigawa et al., 2024). Therefore, dual stimulation of the positive (umami/sweet) and negative (bitter) pathways may result in a mixed sensory experience, thereby limiting the net palatability of diets enriched with these amino acids. This finding contrasts with the more selective interactions observed for lysine,

histidine, glutamine, and glutamic acid, which preferentially target sweet and umami receptors while avoiding strong activation of bitter receptors. Such selective receptor engagement provides a clearer molecular rationale for why these amino acids may be more effective drivers of palatability in canine diets, offering a taste profile that reinforces positive sensory cues without simultaneously triggering aversion. The distinction between broadly binding amino acids and those with selective receptor preferences is an important finding, as it provides a mechanistic explanation for why certain amino acids can effectively contribute to the acceptance of dog food formulations. Moreover, the selective activation of umami and sweet receptors by lysine, histidine, glutamine, and glutamic acid may offer a more targeted strategy for enhancing palatability in future diet design, especially for alternative protein sources or oral drug formulations where masking bitterness is critical. From a nutritional and product development standpoint, these insights are particularly important as the pet food industry increasingly incorporates alternative and non-animal protein sources to improve sustainability. While such proteins may offer environmental benefits, they may lack the same amino acid profiles as traditional animal-derived sources, leading to reduced palatability. Understanding which amino acids most effectively stimulate umami and sweet receptors provides a rational basis for designing palatability enhancers tailored for canine diets.

Conclusion

This study establishes a comprehensive receptor–ligand–based molecular framework for elucidating the determinants of taste perception and palatability in dogs, with a specific focus on the role of amino acids in activating umami and sweet taste receptors. Docking all twenty naturally occurring amino acids against the full set of currently identified canine taste receptors revealed distinct patterns of receptor selectivity, which clarify why particular protein sources and amino acid profiles elicit stronger feeding responses in dogs. The results demonstrate that lysine, histidine, glutamine, glutamic acid, and arginine are the most effective co-stimulators of umami and sweet receptors, exhibiting stronger and more selective binding than many other amino acids. In contrast, amino acids such as tyrosine, tryptophan, and phenylalanine, while

displaying high overall affinity, interact with multiple receptor classes, including bitter receptors, which may diminish their overall contribution to palatability. These findings indicate that selective activation of nutrient-associated taste pathways, rather than general receptor binding strength, is a critical factor in enhancing food acceptance in dogs.

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