

Sodium-glucose cotransporter 2 inhibitors versus insulin therapy in companion animals with diabetes mellitus: a systematic review of current evidence and therapeutic perspectives.

Luminița Diana HRIȚCU¹, Eugenia DUMITRESCU^{2*}, Florin NECHIFOR^{1*}, Vasile BOGHIAN¹, Ioana Ștefania CUCOȘ¹, Teodor Daniel HRIȚCU¹, Iulia STRATON¹, Marius Stelian ILIE², Alina ANTON¹, Alexandra Andreea Chersunaru¹, Sorin Ioan BEȘCHEA CHIRIAC¹, Mihaela Claudia SPATARU¹.

¹Ion Ionescu de la Brad University of Agricultural Sciences and Veterinary Medicine of Iași, 3 Mihail Sadoveanu Alley, 700490 Iași, România, e-mail: luminita.hritcu@iuls.ro; florin.nechifor@iuls.ro; vasile.boghian@iuls.ro; ioana.cucos@iuls.ro; teodor.hritcu@iuls.ro; iulia.straton@iuls.ro; alina.anton@iuls.ro; alexandra.chersunaru@iuls.ro; sorin.beschea@iuls.ro; mihaela.spataru@iuls.ro.

²University of Life Sciences "King Mihai I" from Timisoara Faculty of Veterinary Medicine 119, Calea Aradului, 300645 Timisoara, Romania, e-mail: mariusilie@usvt.ro, eugeniadumitrescu@usvt.ro.

*Correspondence: eugeniadumitrescu@usvt.ro; florin.nechifor@iuls.ro.

Abstract: Diabetes mellitus in companion animals is a growing endocrine disorder in dogs and cats that requires individualized treatment, with insulin therapy remaining the mainstay due to its reliable glycemic control despite certain limitations. SGLT2 inhibitors offer a promising oral alternative for selected cases, while emerging therapies point toward more personalized and advanced future approaches in veterinary diabetology.

Keywords: Diabetes mellitus; SGLT2 inhibitors; insulin therapy.

Introduction: Diabetes mellitus is a common and complex endocrine disorder in dogs and cats, characterized by persistent hyperglycemia due to insulin deficiency, insulin resistance, or both. It shows important species differences canine diabetes resembles human type 1, while feline diabetes is closer to type 2 requiring tailored therapeutic approaches. Its multifactorial nature and growing translational relevance highlight the need for ongoing research and improved management strategies.

Results and Discussions:

1. Comparative Clinical Efficacy

Insulin remains the standard therapy in both dogs and cats, providing effective glycemic control at all stages of the disease, while SGLT2 inhibitors represent a promising alternative only in stable feline patients, with comparable efficacy in selected cases.

Parameter	Insulin therapy	SGLT2 inhibitors
Mechanism of action	Insulin replacement	Insulin-independent glucose excretion
Species applicability	Dogs & cats	Primarily cats
Glycemic control	Highly effective (gold standard)	Comparable in selected stable feline cases
Administration	Injectable (1–2 times/day)	Oral (once daily)
Compliance	Moderate–low	High
Clinical stability requirement	Works in all stages	Requires stable diabetes
Evidence in dogs	Strong	Very limited / not recommended
Evidence in cats	Strong	Emerging but promising

Table 1. Comparative efficacy of SGLT2 inhibitors vs insulin therapy in companion animals with diabetes mellitus.

2. Safety and Adverse Effects

Insulin is primarily associated with the risk of hypoglycemia, whereas SGLT2 inhibitors have a lower hypoglycemia risk but may induce euglycemic ketoacidosis and dehydration.

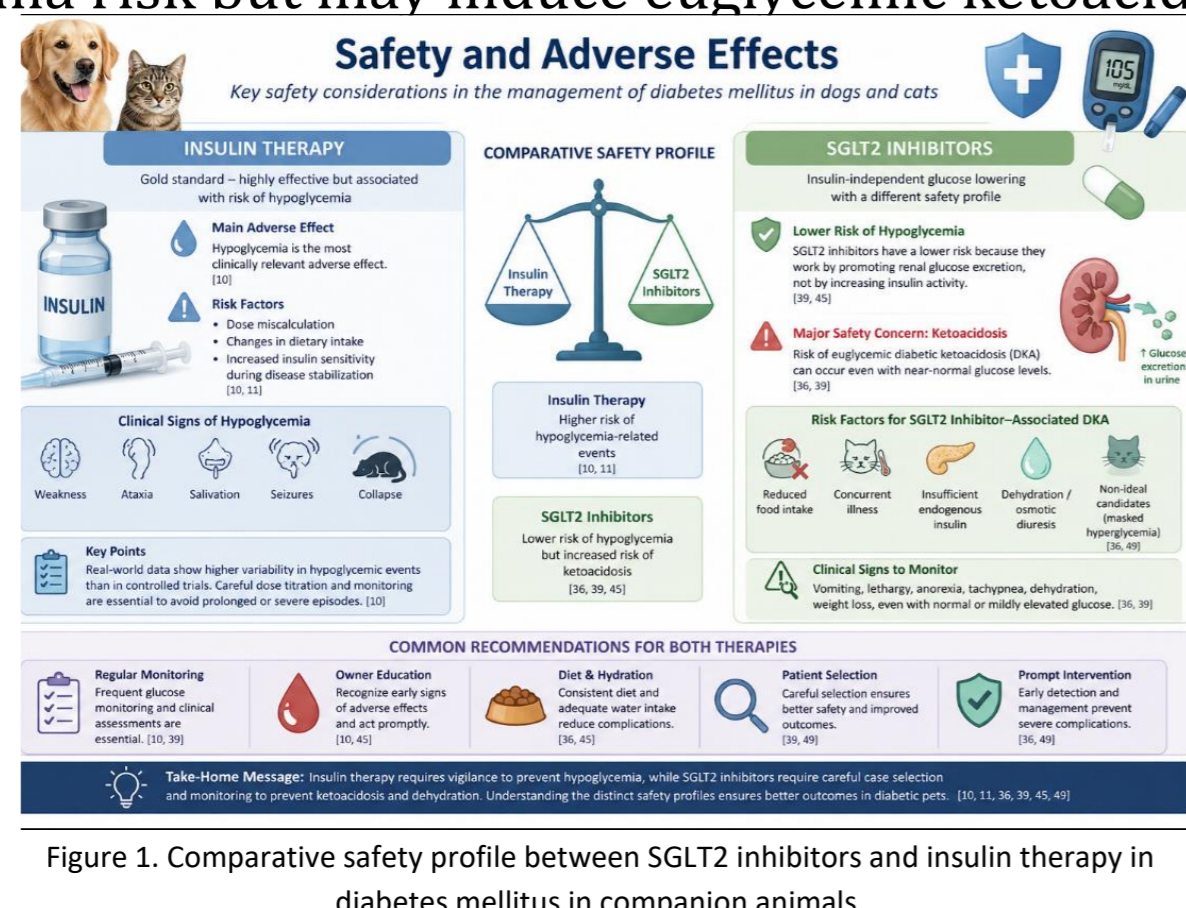


Figure 1. Comparative safety profile between SGLT2 inhibitors and insulin therapy in diabetes mellitus in companion animals.

3. Species-Specific Differences

Diabetes differs significantly between dogs and cats, with dogs being mostly insulin-dependent and cats commonly showing insulin resistance and potential remission, requiring different therapeutic approaches.

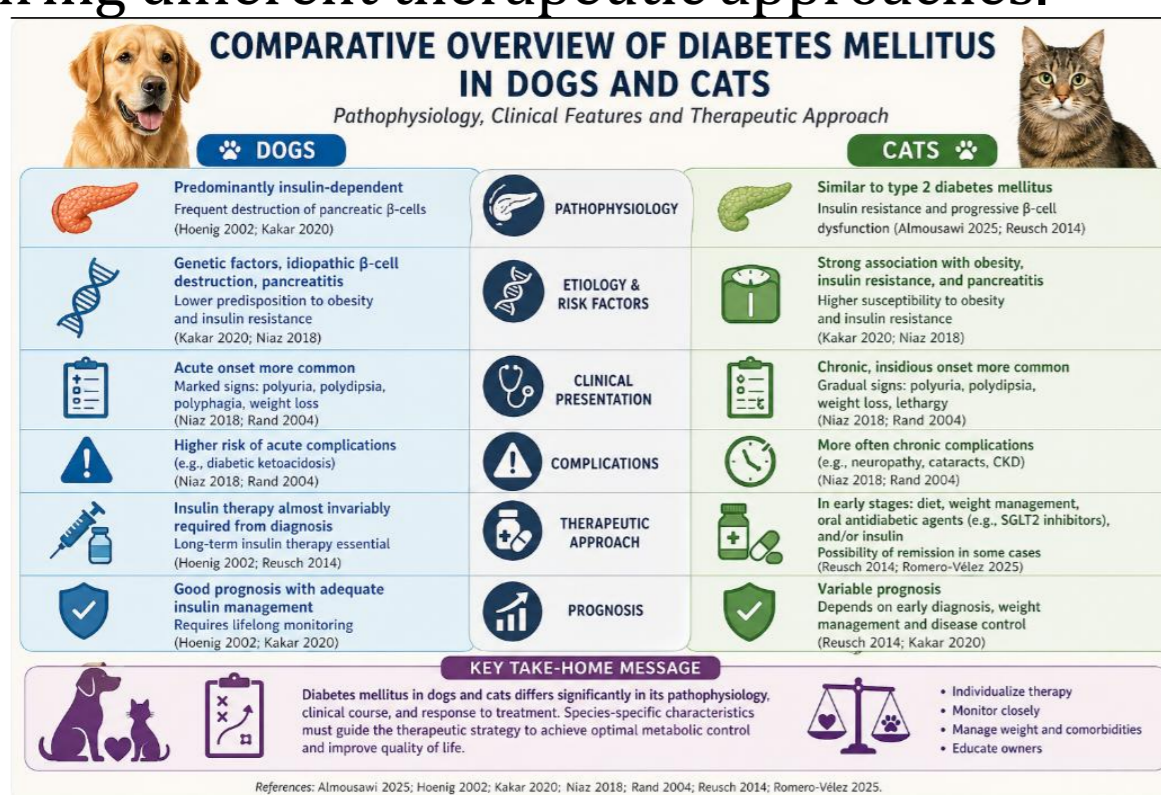


Figure 2. Differences in Diabetes Mellitus Between Dogs and Cats: A Comparative Diagram.

4. Advantages and Limitations

Insulin provides proven efficacy and broad applicability but requires injections and monitoring, while SGLT2 inhibitors improve compliance through oral administration but are limited by metabolic risks and restricted indications.

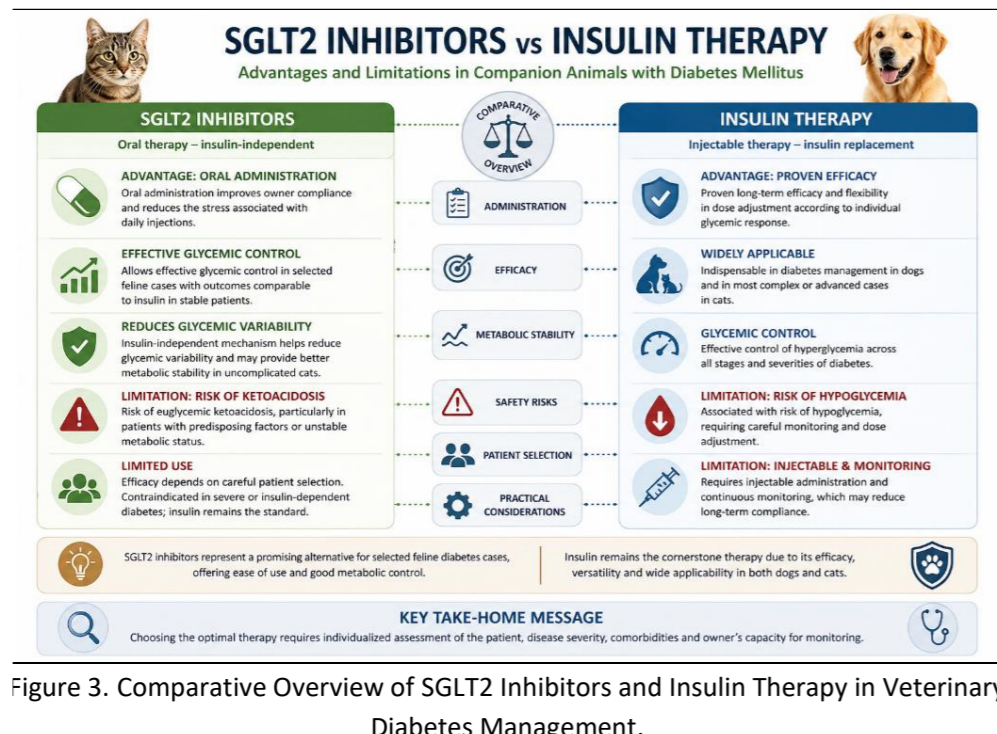


Figure 3. Comparative Overview of SGLT2 Inhibitors and Insulin Therapy in Veterinary Diabetes Management.

Materials and Methods:

- This systematic review compares the efficacy and safety of SGLT2 inhibitors and insulin therapy in diabetic dogs and cats using data from major scientific databases.
- Relevant clinical studies were selected based on predefined criteria after a structured screening process.
- Data were analyzed qualitatively, focusing on efficacy, safety, and species-specific responses.

5. Factors Influencing Therapeutic Choice

Therapeutic choice is influenced by multiple factors, including species, pathophysiology, comorbidities, hepatic function, pharmacology, clinician experience, and owner compliance.

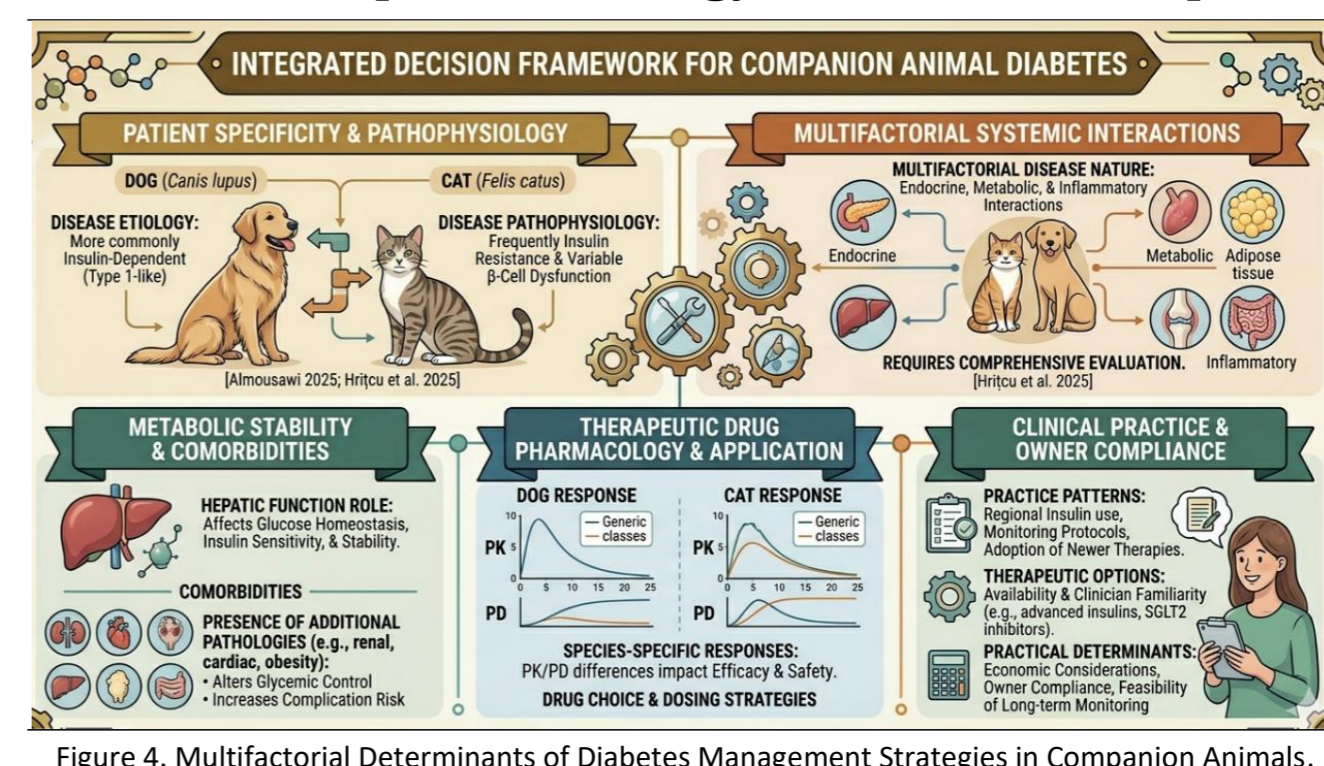


Figure 4. Multifactorial Determinants of Diabetes Management Strategies in Companion Animals.

6. Limitations of Current Evidence

Current evidence is limited by the lack of large clinical trials, data heterogeneity, and insufficient long-term information, especially for newer therapies.

7. Therapeutic Perspectives and Future Directions

Future therapies (stem cells, gene therapy, GLP-1 analogs, advanced insulin formulations) show promising potential for more effective and personalized treatments but remain in early stages.

Therapeutic Approach	Mechanism / Concept	Potential Advantages	Current Limitations
Stem cell therapy	Regeneration of insulin-producing cells	Potential β-cell restoration, improved glycemic control	Experimental stage, limited veterinary trials [Bhansali et al. 2017]
Gene therapy	Genetic modulation of insulin/glucose pathways	Long-term metabolic correction, reduced insulin dependence	High complexity, limited clinical availability [Callejas et al. 2013]
Neo-islet transplantation	Stem cell + islet cell aggregates	Restoration of endogenous insulin secretion	Early-stage studies, unknown long-term safety [Goode et al. 2019]
GLP-1 analogs	Enhancement of insulin secretion and satiety regulation	Improved glycemic control, reduced insulin needs	Limited veterinary approval and data [Gilor et al. 2016]
Ultra-long-acting insulin	Extended pharmacokinetic profile	Reduced injection frequency, better compliance	Cost, limited availability [Reinhart & Graves 2023]
SGLT2 inhibitors	Renal glucose excretion	Oral administration, insulin-independent control	Risk of ketoacidosis, careful selection required [Romero-Vélez et al. 2025]
Advanced insulin delivery systems	Optimized formulations and dosing systems	Improved stability and glycemic control	Need for monitoring and owner training [Susi et al. 2025]

Table 2: Emerging and Future Therapeutic Strategies in Companion Animal Diabetes.

Conclusions

Diabetes mellitus in companion animals requires an individualized, species-specific approach, with insulin remaining the mainstay therapy despite its limitations, while SGLT2 inhibitors offer a promising oral alternative in selected feline cases, and future management is expected to evolve toward more personalized strategies supported by emerging therapies that still require further validation.

References

- Adin, C. A., & Gilor, C. (2017). The diabetic dog as a translational model for human islet transplantation. *The Yale journal of biology and medicine*, 90(3), 509.
- Hrițcu LD, Pavel G, Hrițcu TD, Nechifor F, Boghian V, Anton A, Cucos IS, Chersunaru AA, Munteanu A, Spătaru MC. Comparative oxidative stress in diverse endocrine disorders to pets. *Scientific Papers. Series Veterinary Medicine*. 2025;68(4): 17-27.
- Hrițcu LD, Pavel G, Nechifor F, Hrițcu TD, Cucos IS, Boghian V, Drugociu DG, Roșca P, Beșchea Chiriac SI, Spataru MC. Acute urinary retention associated with diabetic autonomic neuropathy in a cat with type 2 diabetes mellitus and a benign mammary tumour – case report. *Rev Rom Med Vet*. 2026;36(1):5–10.
- Hrițcu, L. D., Boghian, V., Pavel, G., Hrițcu, T. D., Nechifor, F., Spataru, A., ... & Spataru, M. C. (2025). Systematic Review: Exploring Inter-Species Variability in Diabetes Mellitus for Translational Medicine. *Life*, 16(1), 64.
- HRIȚCU, T. D., CUCOȘ, I. Ș., HRIȚCU, L. D., SPĂTARU, M., SOLCAN, G., & ANTON, A. (2024). THE IMPACT OF CORTISOL ON DIVERSE ENDOCRINE PATHOLOGIES IN COMPANION ANIMALS. *Lucrari Stiintifice. Seria Medicina Veterinara*, 67(4):100-114.
- Hrițcu, T. D., Pavel, G., Tejbán, M., Hrițcu, L. D., & Spataru, M. C. (2025). The impact of hepatic pathology on the regulation mechanism of blood glucose and the role of biochemical markers. *Rev Rom Med Vet*, 35(4), 27-33.
- Hrițcu, T. D., Pavel, G., Vornicu, I., Spătaru, A., Hrițcu, L. D., Roșca, P., ... & SPĂTARU, M. C. (2025). Multifactoriality of diabetes mellitus in companion animals: Predisposing factors, triggers, and bidirectional interactions with other pathologies. *Int Quintessence Biomed Res*, 2(3), 245-259.