

COMMENTARY TO HABILITATION THESIS¹

The aim of my thesis is to find compounds with antioxidant, anti-inflammatory, and antidiabetic effects that could help in the treatment of hyperglycemia in patients with type 2 diabetes mellitus (T2DM) and alleviate its long-term complications. In the introduction I briefly describe my field “molecular pharmacy” and all my other publications. The second part focuses on the pathophysiology of T2DM. The third part concentrates on various natural phenolics and their antioxidant, anti-inflammatory, and antidiabetic effects, and a comparison of the different methods that are used to determine these. The last subchapter deals with the encapsulation of natural phenolics to improve their solubility. The concept of “one compound with a combination of effects” is shown on a model compound – the geranylated flavanone diplacone.

Diabetes mellitus (DM) is a chronic metabolic disease with high morbidity and mortality. Its symptoms are increased thirst, frequent urination, and slow-healing sores. On the biochemical level, the main characteristic of DM is hyperglycemia. There are two basic types of DM: type 1 (T1DM), caused by an absolute deficiency of the hormone insulin, and type 2 (T2DM), in which the blood level of insulin is normal, but its effect is suppressed by insulin resistance. According to the International Diabetes Federation (IDF), 537 million adults were living with DM in 2021, and the number is projected to rise to 783 million by 2045.

This thesis is a collection of 12 peer-reviewed papers published between 2010 and 2025. All the papers concentrate on the effects of natural phenolics on alleviating the symptoms or complications of T2DM. The first 5 papers describe their antioxidant effects¹⁻⁵, the following 2 papers focus on their anti-inflammatory potential^{6,7}, 2 papers concentrate on the antidiabetic effects^{8,9}, and finally, 3 papers describe the encapsulation of natural phenolics¹⁰⁻¹² to enhance their solubility and biological activity.

The key question of my research is: “*Are there any natural phenolic compounds that are effective as antioxidant, anti-inflammatory, and antidiabetic agents?*” As proof of this concept, the geranylated flavanone diplacone was highlighted throughout the thesis.

¹ The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant’s contribution in terms of both quality and content.

1) **Treml, J.**; Smejkal, K. Flavonoids as Potent Scavengers of Hydroxyl Radicals. *Comprehensive Reviews in Food Science and Food Safety* 2016, 15, 720-738 (IF = 5.974).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	-	75	50

2) Zima, A.; Hosek, J.; **Treml, J.**; Suchy, P.; Prazanova, G.; Lopes, A.; Zemlicka, M. Antiradical and Cytoprotective Activities of Several C-Geranyl-substituted Flavanones from *Paulownia tomentosa* Fruit. *Molecules* 2010, 15, 6035-6049 (IF=1.988).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
35	-	25	25

3) **Treml, J.**; Smejkal, K.; Hosek, J.; Zemlicka, M. Determination of antioxidant activity using oxidative damage to plasmid DNA - pursuit of solvent optimization. *Chemical Papers* 2013, 67, 484-489 (IF=1.193).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
100	-	80	50

4) **Treml, J.**; Lelakova, V.; Smejkal, K.; Paulickova, T.; Labuda, S.; Granica, S.; Havlik, D.; Padrtova, T.; Hosek, J. Antioxidant Activity of Selected Stilbenoid Derivatives in a Cellular Model System. *Biomolecules* 2019, 9, 468 (IF=4.082).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	50	75	50

5) **Treml, J.**; Vecerova, P.; Herczogova, P.; Smejkal, K. Direct and Indirect Antioxidant Effects of Selected Plant Phenolics in Cell-Based Assays. *Molecules* 2021, 26, 2534 (IF=4.927).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
75	50	100	75

6) Malanik, M.; **Treml, J.**; Lelakova, V.; Nykodymova, D.; Oravec, M.; Marek, J.; Smejkal, K. Anti-inflammatory and antioxidant properties of chemical constituents of *Broussonetia papyrifera*. *Bioorganic Chemistry* 2020, 104, 104298 (IF=5.275).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	50	25	25

7) Molcanova, L.; **Treml, J.**; Brezani, V.; Marsik, P.; Kurhan, S.; Travnicek, Z.; Uhrin, P.; Smejkal, K. C-geranylated flavonoids from *Paulownia tomentosa* Steud. fruit as potential anti-inflammatory agents. *Journal of Ethnopharmacology* 2022, 296, 115509 (IF=5.400).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	-	25	25

8) **Treml, J.**; Nykodýmová, D.; Kubatka, P. Phytochemistry Reviews 2025, doi: 10.1007/s11101-025-10121-w (IF=7.300).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	25	90	100

9) **Treml, J.**; Václavík, J.; Molčanová, L.; Čulenová, M.; Hummelbrunner, S.; Neuhauser, C.; Dirsch, V. M.; Weghuber, J.; Šmejkal, K. Structure activity relationship of flavonoids as PPAR γ agonists. *Journal of Agricultural and Food Chemistry* 2025, doi: 10.1021/acs.jafc.4c11398 (IF=5.700)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40	-	90	100

10) **Treml, J.**; Salamunova, P.; Hanus, J.; Hosek, J. The effect of curcumin encapsulation into yeast glucan particles on antioxidant enzyme expression *in vitro*. *Food & Function* 2021, 12, 1954-1957 (IF=6.317).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
75	-	80	25

11) Salamunova, P.; Cupalova, L.; Majerska, M.; **Treml, J.**; Ruphuy, G.; Smejkal, K.; Stepanek, F.; Hanus, J.; Hosek, J. Incorporating natural anti-inflammatory compounds into yeast glucan particles increases their bioactivity *in vitro*. *International Journal of Biological Macromolecules* 2021, 169, 443-451 (IF=8.025).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	50	25	25

12) Nykodýmová, D.; Molčanová, L.; Kotouček, J.; Mašek, J.; **Treml, J.** PPAR γ Agonistic Activity of Mimulone and Diplacone Encapsulated in Liposomes and Cyclodextrin Complexes. *ChemistryOpen* 2025, doi: 10.1002/open.202500209 (IF=3.100).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
-	75	25	50