

Highlights

- Apigenin has the highest *in silico* and *in vitro* antithyroid activity among all identified *Medicago sativa* L. sprouts phytoconstituents.
- Apigenin *in vivo* antithyroid mechanism is mainly via inhibition of TPO and more prominently, IDI-1.
- Apigenin therapy was superior to PTU in achieving nearly euthyroid state (without incidence of hypothyroidism or thyroid gland hypertrophy or hyperplasia).
- In addition, apigenin, but not PTU, corrected hyperthyroidism-induced LVH without noteworthy liver toxicity or reduction of WBCs count.
- Thus, apigenin may represent a possible safer alternative to conventional antithyroid drugs.