



The 7th International Electronic Conference on Medicinal Chemistry (ECMC 2021)

01-30 NOVEMBER 2021 | ONLINE

Thyme as a perspective antioxidant agent with antidiabetic and antitumor potential

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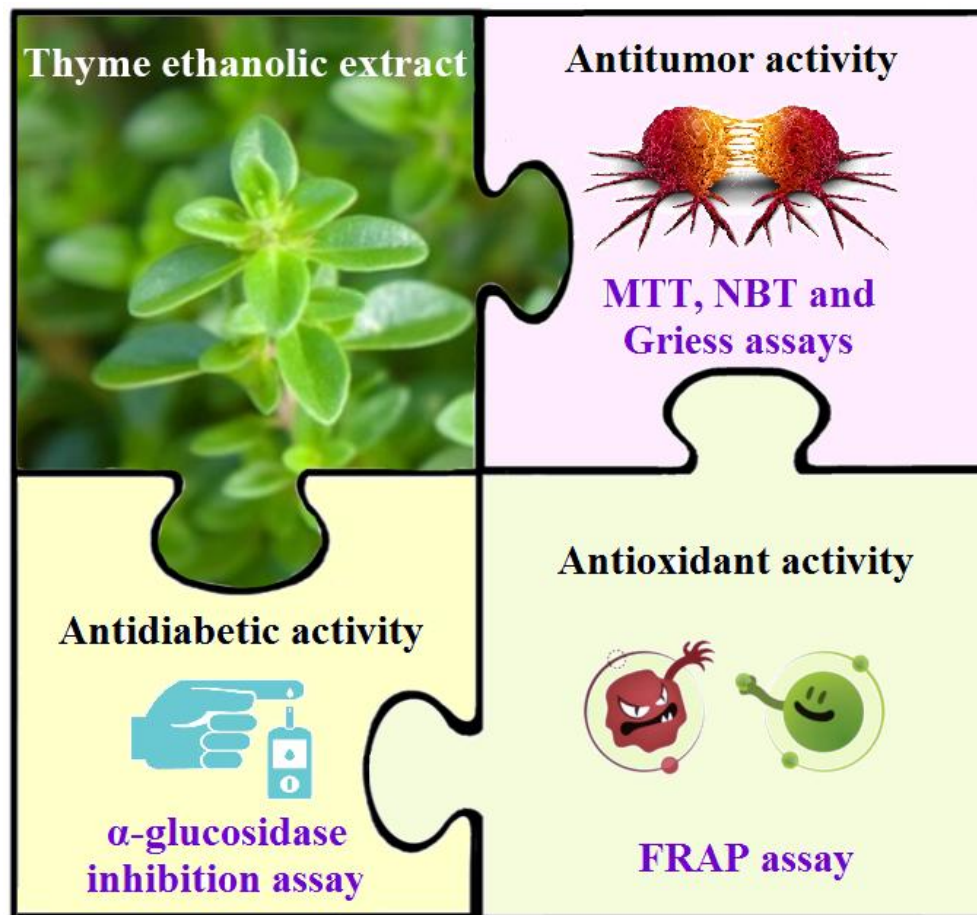
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Graphical Abstract



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Abstract:

Type 2 diabetes (T2D) increases the incidence of **colorectal cancer** up to three times compared to the population without T2D. **Oxidative stress**, which is a promoting factor in both conditions, can be efficiently reduced by bioactive compounds from natural sources. Hence, this study aimed to test whether the ethanolic extract of ***Thymus vulgaris* (thyme)** tested at 100 µg/mL can act as an effective antioxidant, antidiabetic, and antitumor agent. Plant material was provided by the Institute for Medicinal Plant Research “Dr. Josif Pančić”, Serbia. The antioxidant activity was tested using FRAP assay; the antidiabetic effect was assessed by the level of α -glucosidase inhibition, while the antitumor activity towards colorectal cancer (HCT-116) cell line was determined in MTT, NBT, and Griess assays. In FRAP assay, this sample exhibited comparable antioxidant activity with the one of positive control, BHT (413.03 vs. 576.17 µmol Fe(II)/g dry extract, respectively). Additionally, the extract inhibited 25.91% of α -glucosidase activity, while the standard, acarbose, inhibited 36.76% of α -glucosidase. Although the extract did not influence the viability of HCT-116 cells, it significantly elevated the production of reactive oxygen species (ROS) and nitric oxide (NO) by these cells compared to the untreated control, indicating potential antitumor activity. Finally, **thyme ethanolic extract exhibited significant antioxidant and anti- α -glucosidase activities *in vitro*, as well as ROS- and NO-modulating effects in HCT-116 cells**, hence it can be considered as a promising agent for further examination of its action mechanisms in more complex model systems.

Keywords: antidiabetic activity; antioxidant activity; antitumor activity; colorectal cancer; *Thymus vulgaris* extract



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Introduction

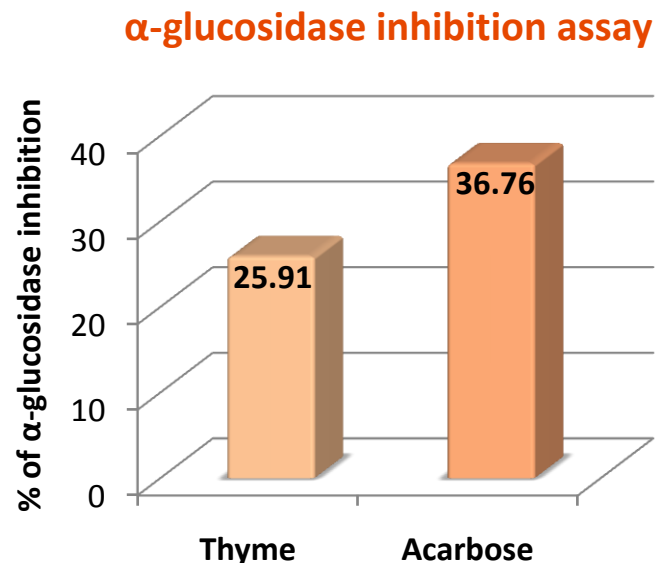
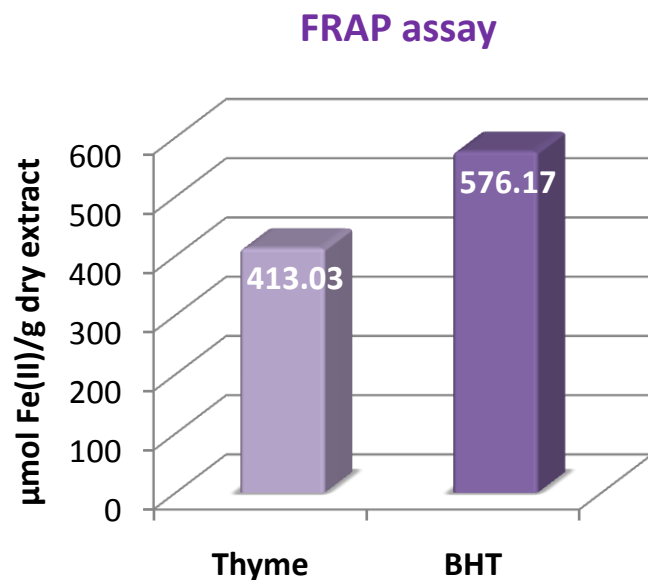
- **The production of free radicals**, such as reactive oxygen (ROS) and nitrogen species (RNS), is **genetically programmed** since they function as **key signaling molecules** that protect the body and alleviate inflammatory processes.
- If their production exceeds the antioxidant capacity of the cell, these radicals begin to **oxidize essential biomolecules of the cell** such as proteins, lipids, and DNA, leading to **oxidative stress**.
- Oxidative stress is linked to a plethora of diseases, **diabetes and cancer** being among them.
- There is a growing interest in **nutraceuticals** nowadays, which have the potential to **restore the imbalance** caused by oxidative stress, to regenerate the non-tumor tissue, and also induce cancer cell death.
- **Species from the Lamiaceae family** represent powerful antioxidants due to the fact that they are rich in bioactive compounds such as **polyphenols and terpenes**.



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Results and Discussion

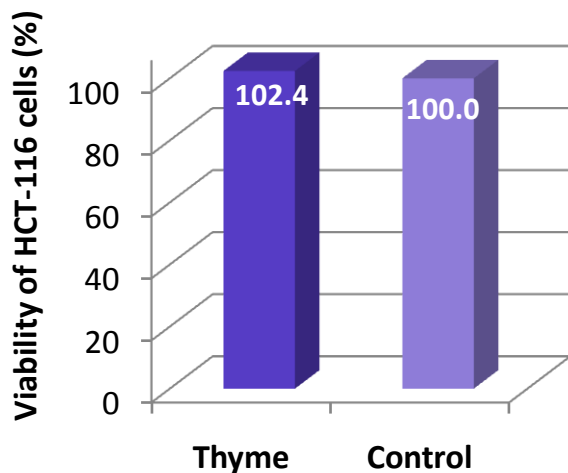


- The **antioxidant** and **antidiabetic** activities of thyme ethanolic extract were comparable with the positive controls, BHT and acarbose, tested at the same concentrations.
- These results are **in agreement with the existing literature data** since thyme is a well-known antioxidant and antidiabetic agent, however **its effects on α -glucosidase have not been reported previously.**

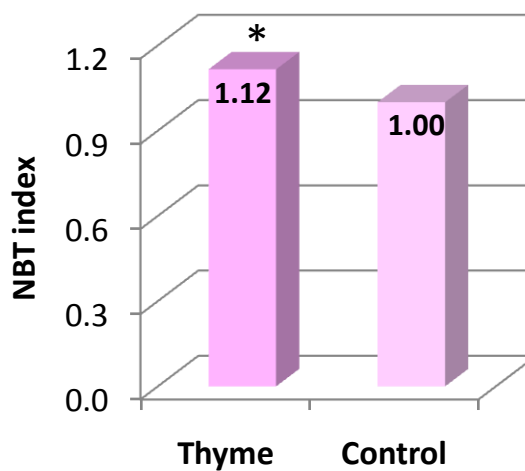


Results and Discussion

MTT assay

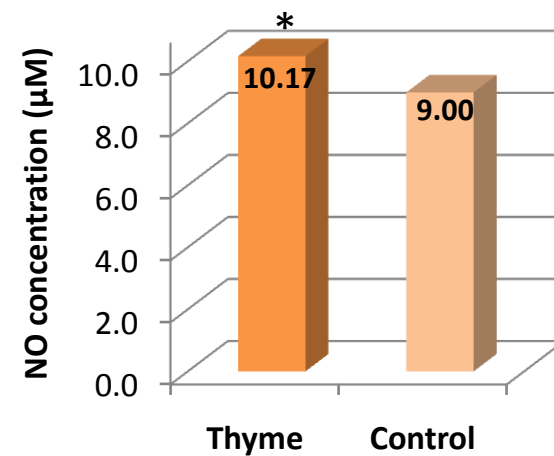


NBT assay



* $p < 0.05$

Griess assay



- Treatment with thyme ethanolic extract **did not reduce the viability** of the HCT-116 cells, however it showed promising antitumor potential by **significantly enhancing the production** of **ROS** and **NO** by the tumor cells in comparison with the untreated control.
- No similar results were found in the available literature, however it is already known that thyme extracts might exert their antitumor action by inhibiting adhesion, migration, and invasive potential of HCT-116 cells.

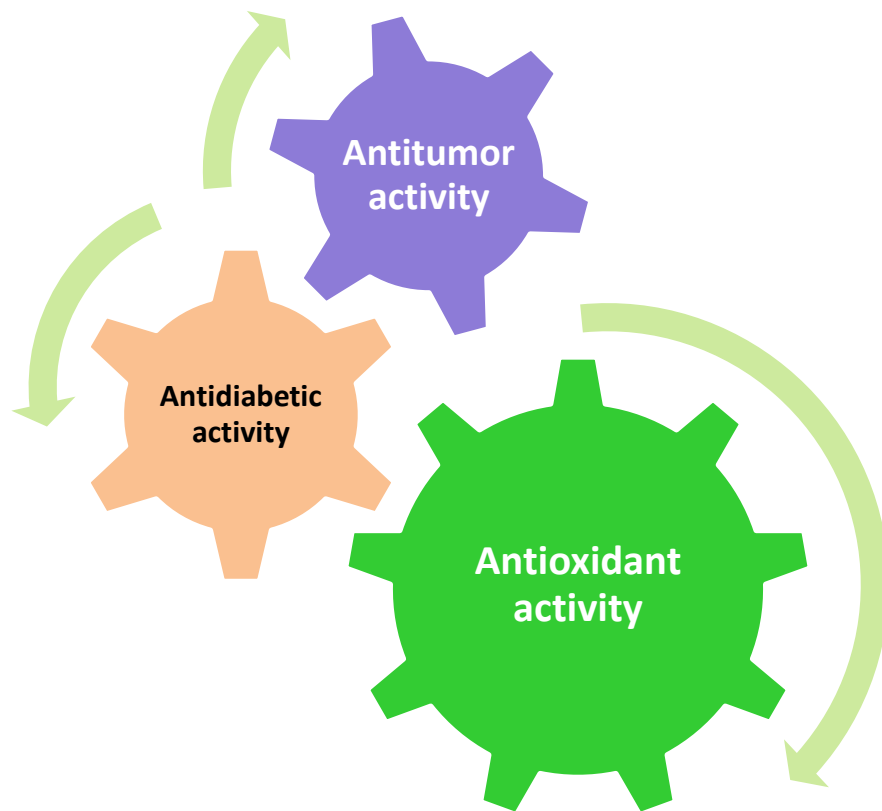


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Conclusions

- Since **oxidative stress** is closely associated with the development of various diseases, timely application of **antioxidant substances** is essential in order to improve the general well-being of the organism.
- **Thyme ethanolic extract** exhibited significant antioxidant and anti- α -glucosidase activities *in vitro*, as well as ROS- and NO-modulating effects in HCT-116 cells.
- Thyme should be considered as a **promising agent for further studies** of its action mechanisms in more complex model systems.



Acknowledgments

The authors are grateful to
the Ministry of Education, Science and Technological Development
of Republic of Serbia
(No. 451-03-68/202014/200178 and 451-03-9/2021-14/200003)
for the financial support



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