

Decoding myrtle activity against Alzheimer's disease: metabolic composition and anti-amyloidogenic activity of myrtle leaves extracts

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The primary challenge when addressing Alzheimer's disease (AD) relies in the significant delay between the molecular onset and the appearance of the first clinical symptoms. For this reason, the development of primary prevention strategies is of fundamental importance. [1] In this context, diet represents a promising preventive tool in addressing AD pathogenesis through a multitargeted approach. [2] Myrtle (*Myrtus communis*) is an evergreen aromatic plant historically employed in cooking and liqueur production; while the leaves are often considered a waste product, they could represent a rich source of bioactive compounds. [3]

Here, we investigate the anti-amyloidogenic activity of the hydro-alcoholic extracts of myrtle leaves against A β 1-42 aggregation, one of the main hallmarks of AD. [4] The combination of advanced analytical techniques (STD NMR to probe molecular interactions and FT-IR/AFM to assess structural and morphological changes) allowed us to demonstrate that myrtle extracts significantly modulate A β 1-42 aggregation. Moreover, in order to identify the compounds responsible for this biological activity, we combined NMR and LC-MS metabolomic approach, which revealed the presence of glycosylated flavonoids, such as myricitrin and other myricetin derivatives, hydrolysable tannins, such as eugeniflorin D2 and oenothien B, and myrtucommulones. These compounds were isolated by preparative HPLC and preliminary tested for their ability to inhibit A β 1-42 aggregation *in vitro*. Overall, our findings suggest that myrtle bioactive compounds are promising nutraceutical candidates for the safe and sustainable prevention of neurodegeneration; their synergistic antioxidant, anti-inflammatory, and anti-amyloidogenic properties allow the effective modulation of early-stage molecular events of Alzheimer's disease. Further studies will be necessary to assess their activity and safety *in vivo*, as well as their ability to prevent the pathological aggregation of other amyloidogenic proteins.

References

- [1]. Guo, J.; Huang, X.; Dou, L.; Yan, M.; Shen, T.; Tang, W.; Li, J. Sig Transduct Target Ther **2022**, 7 (1), 391.
- [2]. Pandey, S. N.; Singh, G.; Semwal, B. C.; Gupta, G.; Alharbi, K. S.; Almalki, W. H.; Albratty, M.; Najmi, A.; Meraya, A. M. Journal of Food Biochemistry **2022**, 46 (12).
- [3]. Tumen, I.; Senol, F. S.; Orhan, I. E. International Journal of Food Sciences and Nutrition **2012**, 63 (4), 387–392.
- [4]. Morante-Carriel, J.; Nájera, H.; Samper-Herrero, A.; Živković, S.; Martínez-Esteso, M. J.; Martínez-Márquez, A.; Sellés-Marchart, S.; Obrebska, A.; Bru-Martínez, R. IJMS **2024**, 25 (23), 13036.

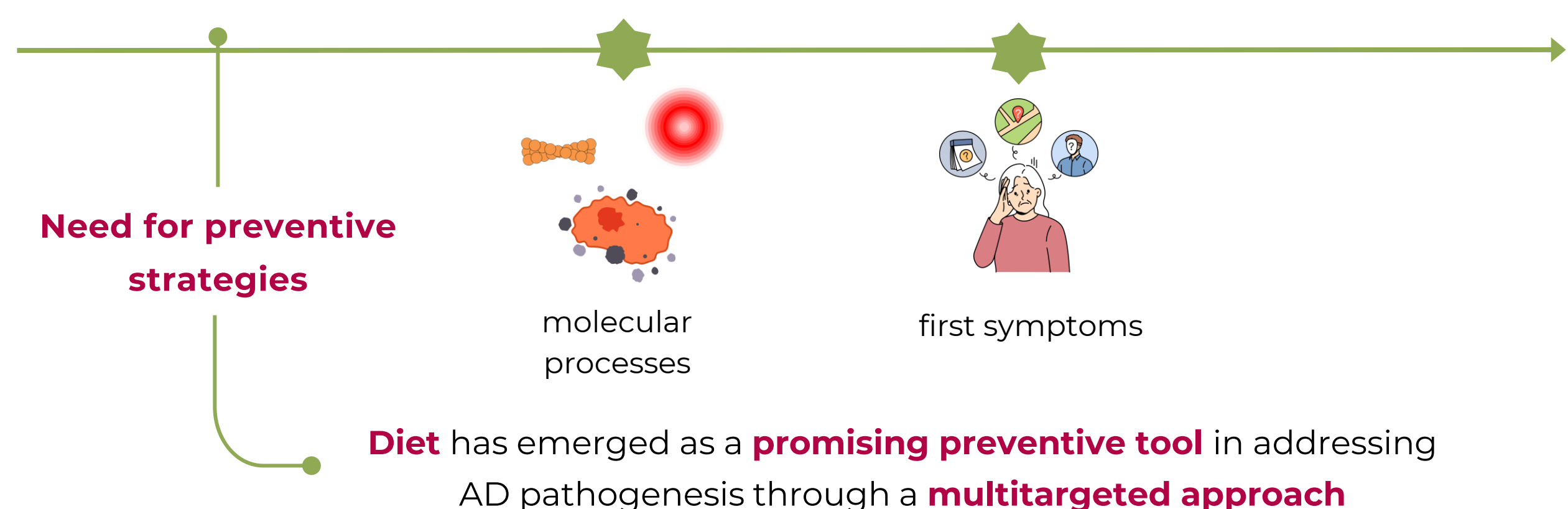
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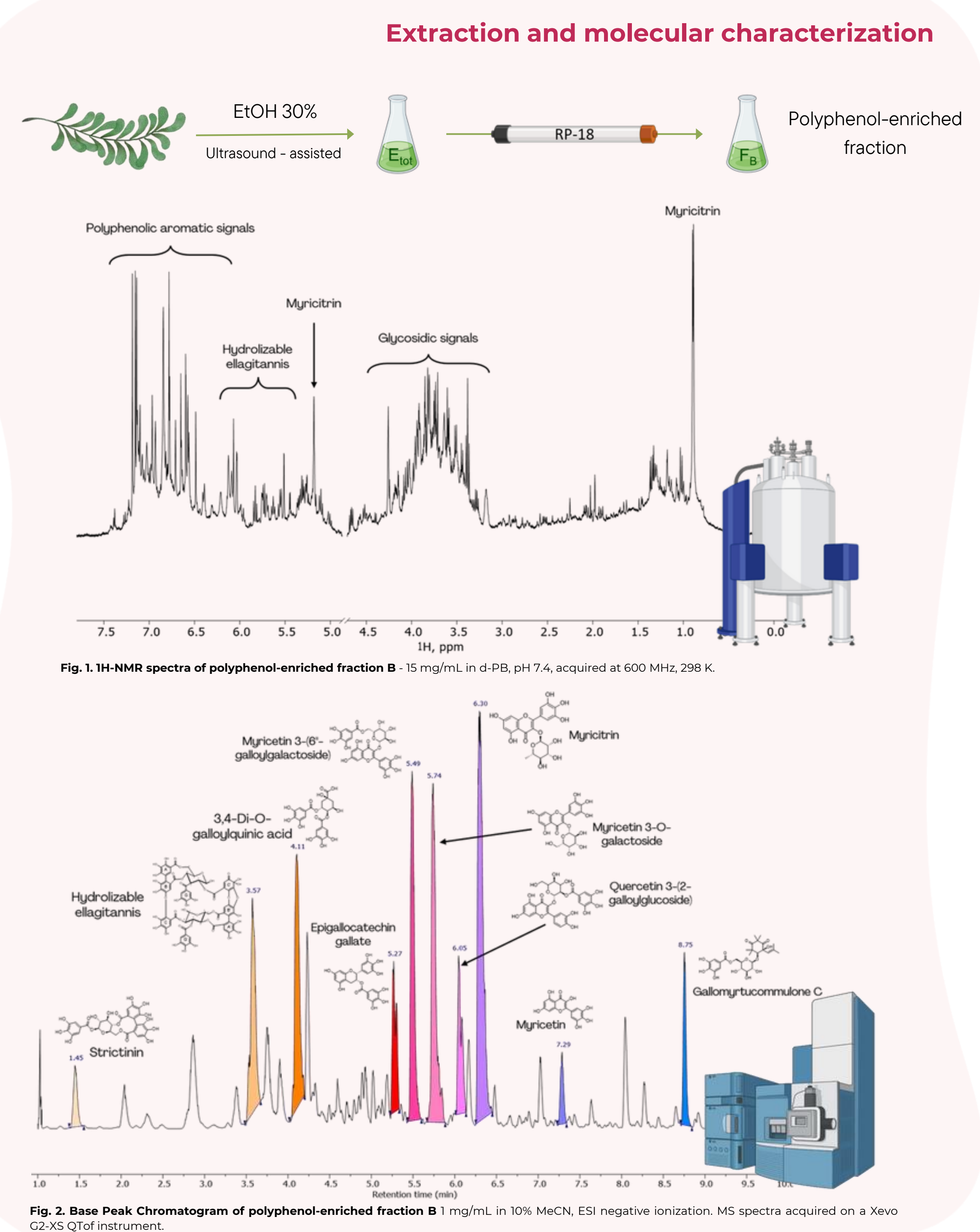
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Alzheimer's disease (AD) is a neurodegenerative disorder caused by the **pathological aggregation of Aβ1-42 peptide**. The main challenge in addressing AD relies in the **delay between the initiation of molecular events and the onset of first clinical symptoms**.



Here, we investigate the **anti-amyloidogenic activity of the hydro-alcoholic extracts of myrtle leaves** against **Aβ1-42 aggregation**, one of the main hallmarks of AD, by combining **different advanced analytical techniques**.



Myrtle (*Myrtus communis*) is an evergreen aromatic plant



Myrtle berries

employed in liqueur production

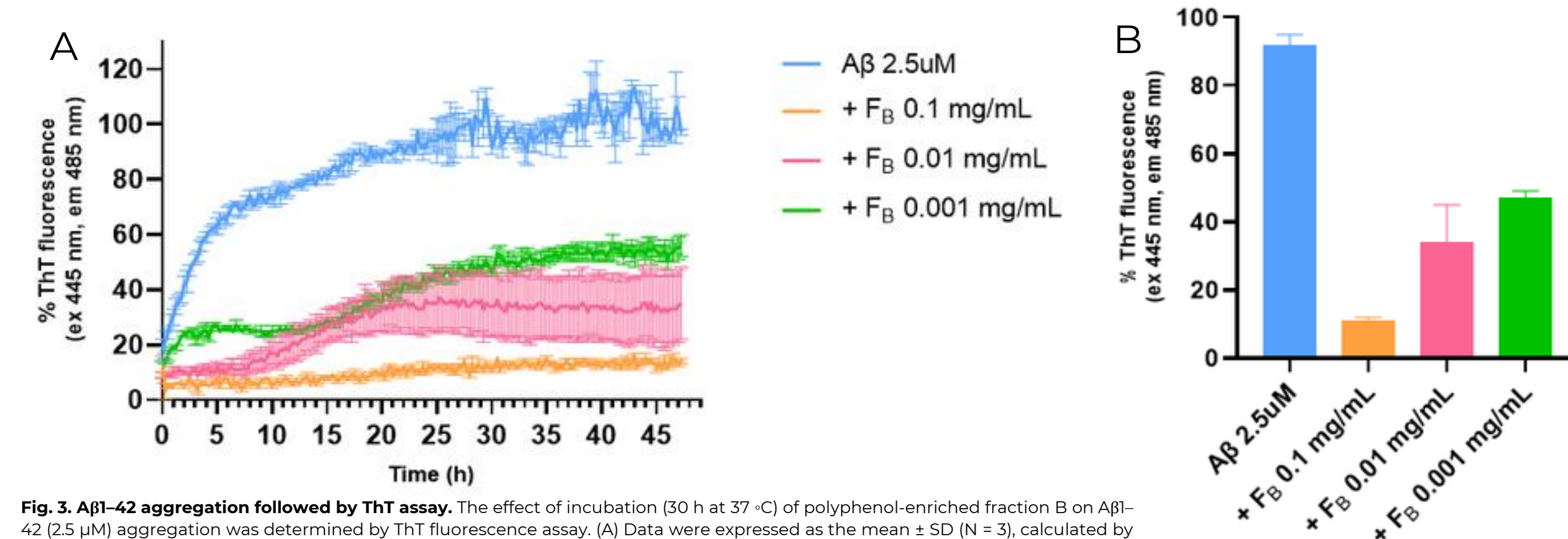


Myrtle leaves

waste product but could represent a **great source of bioactive compounds**

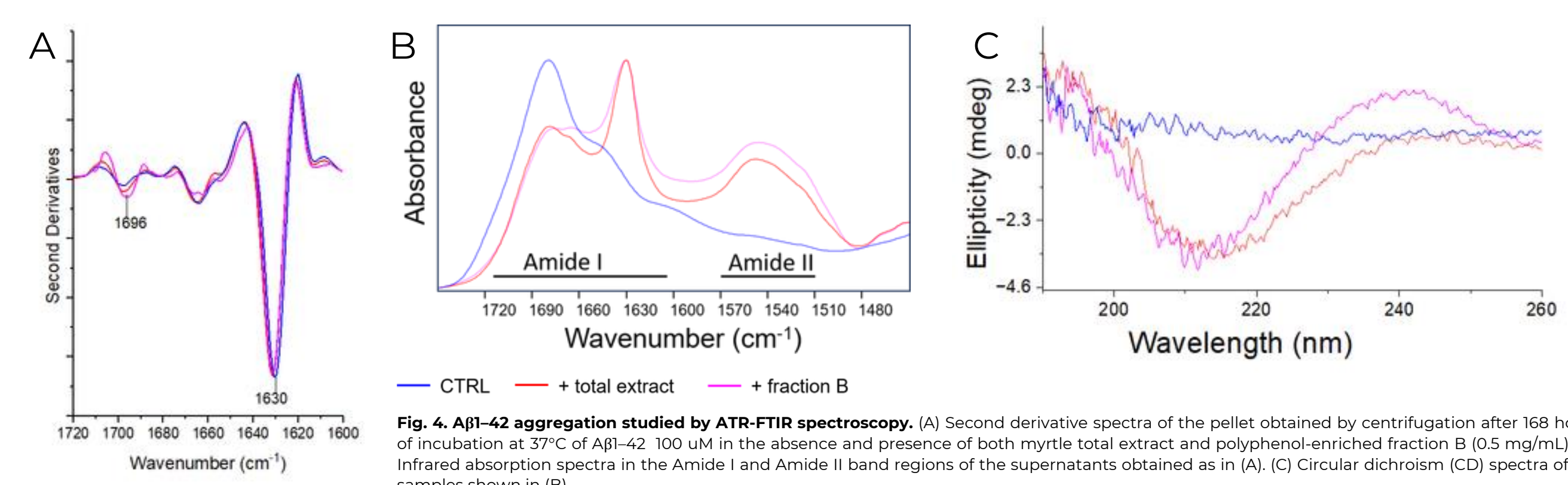


Screening of anti-amyloidogenic activity



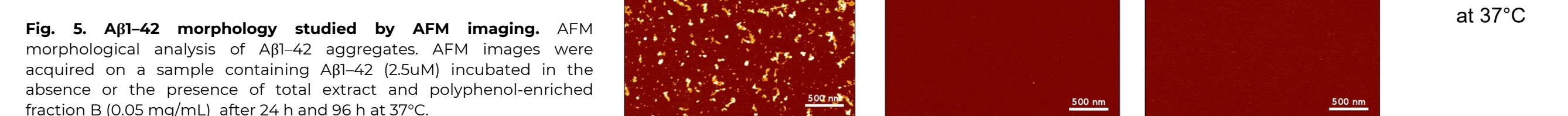
Evaluation of changes in Aβ1-42 secondary structure

Myrtle extracts induce the **formation of soluble and anti-parallel β-sheets aggregates**



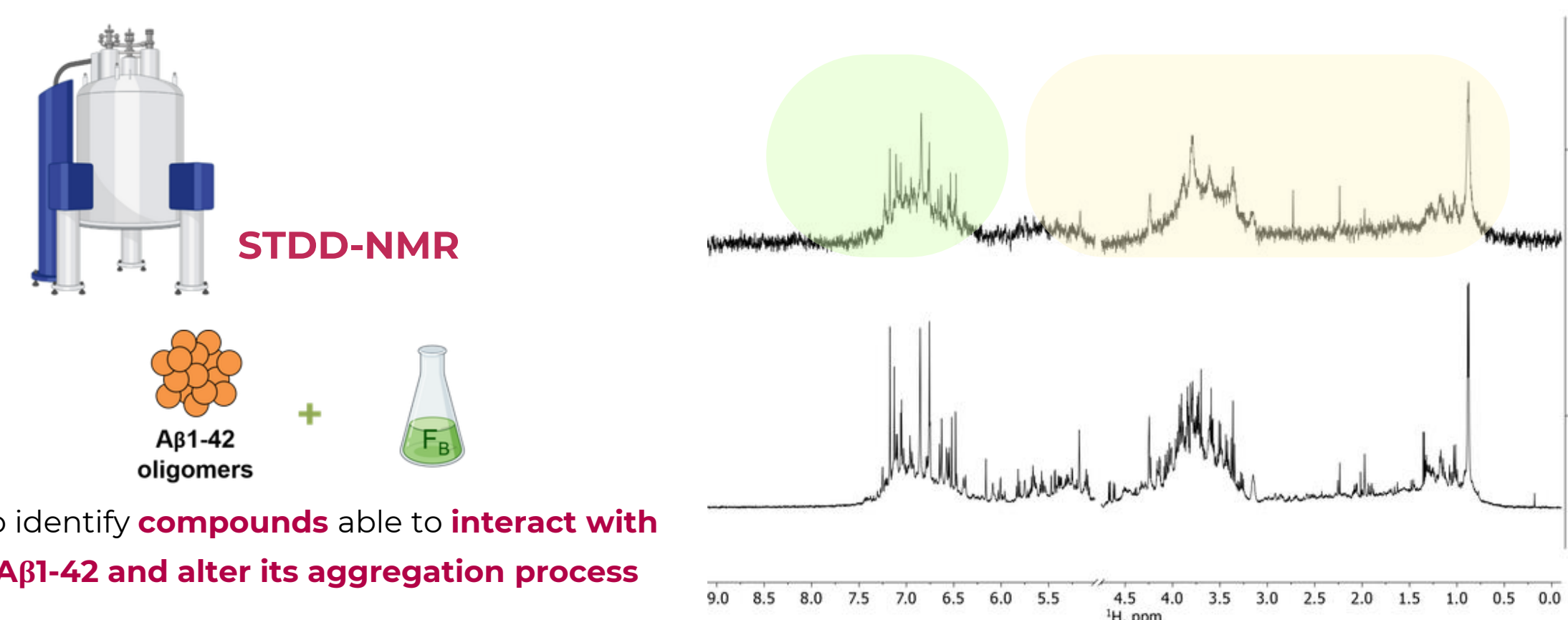
Evaluation of changes in Aβ1-42 morphology

Myrtle leaves extracts **inhibit the formation and stabilization of large fibrillar aggregates**



Which compounds are responsible for biological activity?

Molecular binding is the *conditio sine qua non* for **biological activity**



Conclusions

Myrtle bioactive compounds could be considered promising candidates for **neurodegenerative diseases' prevention**. Their antioxidant, anti-inflammatory and anti-amyloidogenic activity allow the **modulation of molecular events of AD**.



- Guo, J.; Huang, X.; Dou, L.; Yan, M.; Shen, T.; Tang, W.; Li, J. Sig Transduct Target Ther 2022, 7 (1), 391.
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