Inhibitory effect of *Achillea millefolium* on fatty acid amide hydrolase

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Introduction

- Yarrow (*Achillea millefolium*) has an extensive ethnobotanical history in use as a tonic or panacea as well in treating digestive problems and infections , among many other purposes[1]
- Other members of the *Asteraceae* family have already been shown to affect the endocannabinoid system[2]
- Potential therapeutic pathways involving the mammalian endocannabinoid system include treating mood disorders, anxiety disorders, hypertension, and obesity/metabolic disorders, to name only a few[3]
- There is a potential connection between the role of the endocannabinoid system in regulating anxiety and reducing inflammation and the diverse traditional medicinal uses of yarrow
- The fatty acid amide hydrolase enzyme (FAAH) acts to degrade anandamide, a major endogenous activator of the endocannabinoid system[3]

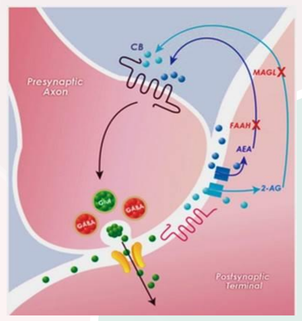

Figure 1. Mammalian endocannabinoid signaling. Image adapted from www.caymanchem.com.

Objectives

- Characterize the effects of yarrow extract on fatty acid amide hydrolase enzyme
- Determine IC_{50} values (the concentration of yarrow extract that inhibits 50% of the enzyme) to compare potencies of different parts of the plant

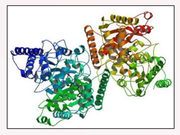

Figure 2. Crystal structure of fatty acid amide hydrolase. Image adapted from www.rcsb.org, structure ID 1MT5.

Results

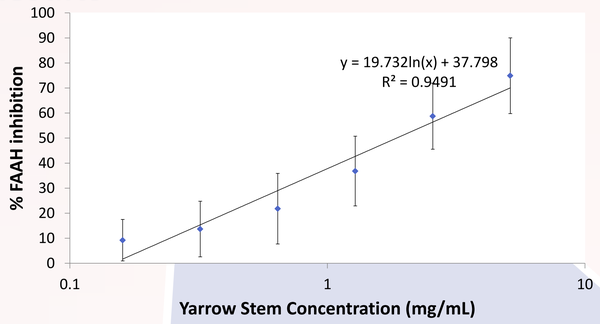

Figure 3. Mean percentage inhibition vs. Yarrow stem extract concentration. Error bars represent means ± one standard error (n = 18).

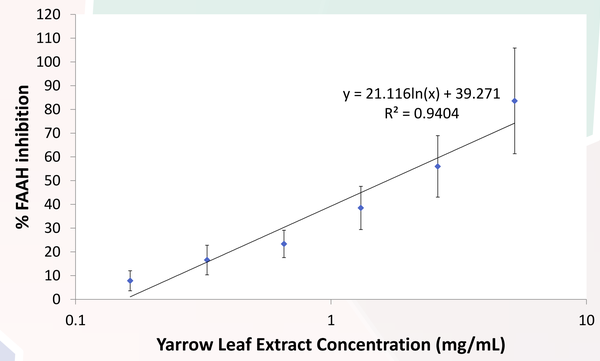

Figure 4. Mean percentage inhibition vs. Yarrow leaf extract concentration. Error bars represent means ± one standard error (n = 18).

- Results indicate that yarrow does inhibit the FAAH enzymes
- Both sets of results fit a logarithmic relationship reasonably well
- Although two different samples of yarrow stem extract were available and tested, this graph includes only the mean of the triplicate from sample 1 because sample 2 gave very low inhibition (see Figure 5 for analysis)

Results

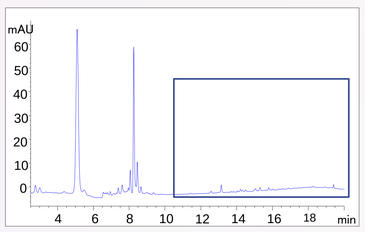

Figure 5A. HPLC analysis of yarrow stem extract 1.

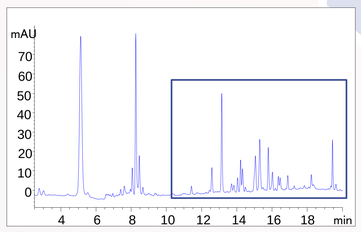

Figure 5B. HPLC analysis of yarrow stem extract 2.

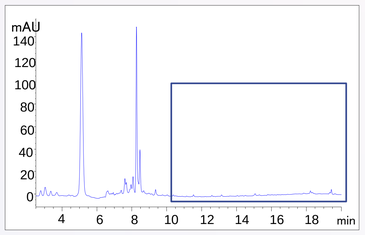

Figure 5C. HPLC analysis of yarrow leaf extract 1.

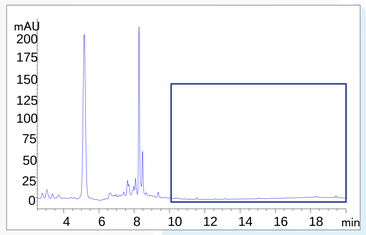

Figure 5D. HPLC analysis of yarrow leaf extract 2.

- Both extracts were made from the same yarrow plant in the same time period
- Chemical profiles of the potent inhibiting stem sample (1) and both leaf samples were similar

Conclusion

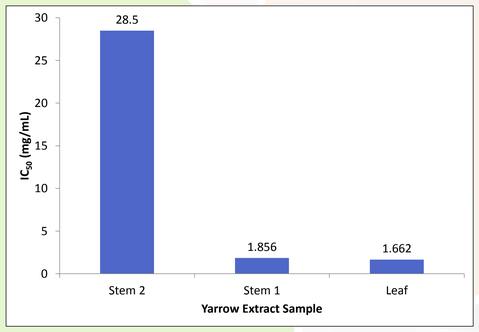

Figure 6. IC_{50} of the stem and leaf samples. This represents the concentration of extract that inhibits 50% of the FAAH enzyme.

- Yarrow leaf presented the most potent inhibition of FAAH, followed closely by the more potent and chemically similar yarrow stem sample
- HPLC analysis indicated a very different chemical profile for the stem sample that was not a potent inhibitor – this provides an explanation for the vastly different IC_{50} results for the two yarrow stem extracts

Methodology

- Yarrow extract samples were dissolved in MeOH and incubated for 60 minutes at 37°C with 12 mM FAAH enzyme and AMC-AA substrate
- JZL 195 was the positive control and 20% MeOH was the vehicle control
- Each of the samples was tested by high performance liquid chromatography for chemical comparison to the yarrow stem sample that was a very poor inhibitor

Future Directions

- Investigate chemical differences between extracts to potentially isolate specific compounds interacting with FAAH
- Determine the effects of yarrow extracts on other endocannabinoid metabolizing enzymes, such as monoacylglycerol lipase (MAGL)
- Characterize the effects of yarrow extracts on cannabinoid receptor signaling

Acknowledgements

I would like to thank Dr. Cory Harris, Rui Lin, and Alexandra Kachura for their support and patience during this project.

References

[1]Applequist, W., & Moerman, D. (2011). Yarrow (*Achillea millefolium L.*): A Neglected Panacea? A Review of Ethnobotany, Bioactivity, and Biomedical Research. *Economic Botany*, 209-225. Retrieved March 8, 2016.

[2]Hajdu, Z., Nicolussi, S., Rau, M., Lorántfy, L., Forgo, P., Hohmann, J., . . . Gertsch, J. (2014). Identification of Endocannabinoid System-Modulating N -Alkylamides from Heliopsis helianthoides var. scabra and Lepidium meyenii. *J. Nat. Prod. Journal of Natural Products*, 77(7), 1663-1669.

[3]Pacher, P., Bátkai, S., & Kunos, G. (2006). The Endocannabinoid System as an Emerging Target of Pharmacotherapy. *Pharmacological Reviews*, 58(3), 389-462.