Mānuka Honey Mead; Worth the Buzz?

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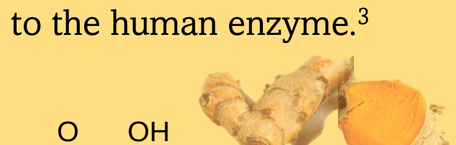
Mead?

Mead is an alcoholic beverage made from fermented honey and water, which has been around since ancient times. While not as prevalent as it once was, mead has seen a resurgence in popularity, largely thanks to TV shows such as Game of Thrones!

Why Mānuka?

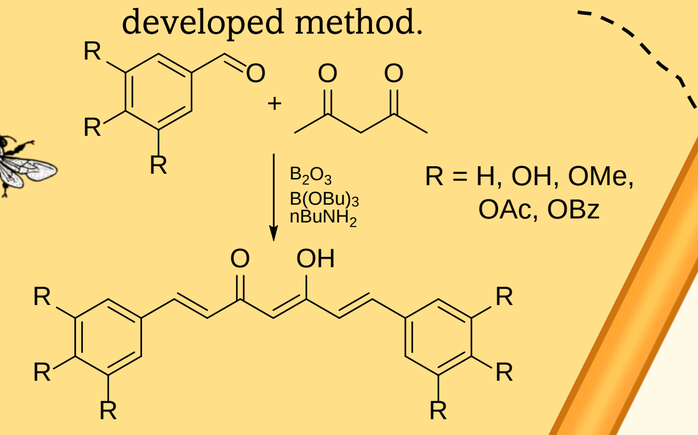
Mānuka honey contains a potent bioactive compound called methyl glyoxal, or MGO.
MGO has significant and well established antibacterial properties,[1] and honeys containing high levels of this compound have very high retail value. A record price of nearly $5,000 per 230 g jar can be found on the shelves at Harrods, London.

MGO



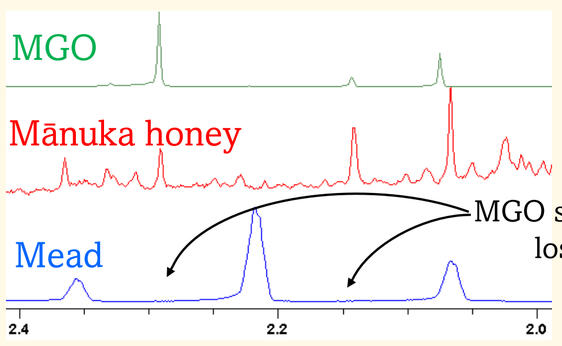
Synthesis of Potential Inhibitors

Based on the modelling results, a selection of compounds most likely to inhibit MGO were synthesised. Nine new compounds were made using this developed method.



Background

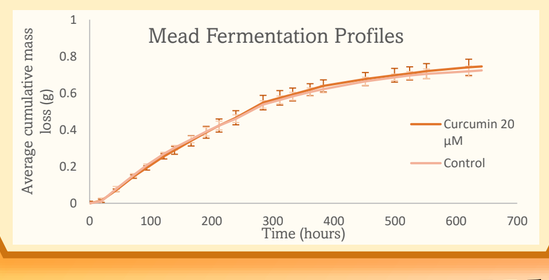
Initial studies showed that when mānuka honey undergoes fermentation by a wine strain of *S. cerevisiae*, the MGO does not persist into the finished mead product.



Fermentations

Initial trial; A series of mānuka honey ferments, inoculated with *S. cerevisiae* wine strain EC-1118, were spiked with curcumin and three of its analogues at 20 μM:

- ✓ Curcuminoid addition did not negatively impact the yeast's fermentative ability.
- ✗ MGO was still not preserved in the mead…

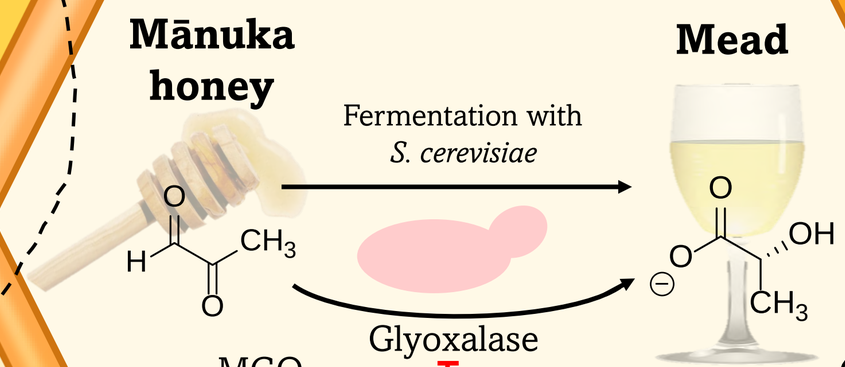


Curcuminoids as Glo1 Inhibitors

Curcumin, the primary active compound in turmeric, is an inhibitor of human Glo1,[2] so we proposed to test it, and other structurally similar compounds, to inhibit Glo1 in yeast, which has significant structural similarities to the human enzyme.[3]

Curcumin

This Research

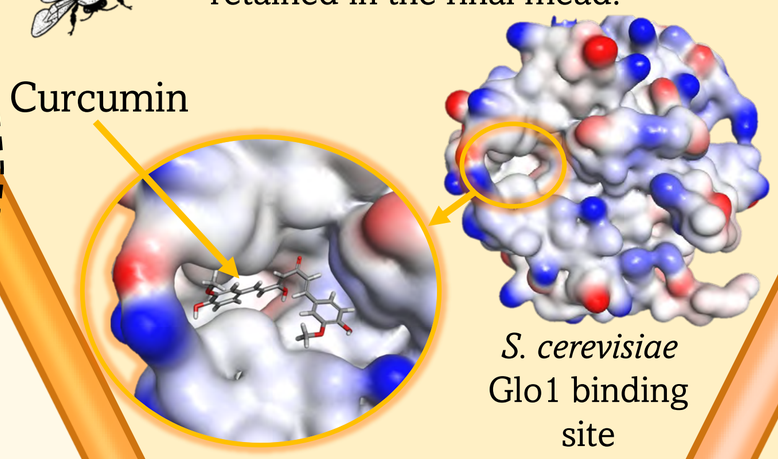


It is suspected that this loss of MGO is the result of a pair of enzymes in the glyoxalase pathway, which metabolise MGO into D-lactate.

To enable the MGO from the honey to persist during fermentation, we proposed to inhibit the first enzyme in this pathway, Glo1, with a natural product based compound.

Molecular Modelling

Molecular models of the binding of a range of curcumin analogues with the *S. cerevisiae* Glo1 enzyme indicated which compounds are more likely to act as inhibitors, thereby helping MGO be retained in the final mead.



S. cerevisiae Glo1 binding site

Next Steps

- Conduct fermentations spiked with higher concentrations of inhibitor than was used in the initial trial.
- Test additional curcumin analogues
- Investigate the use of whole turmeric spice as an inhibitor.
- Investigate spontaneous fermentation with wild yeast present in the honey, alongside inoculated ferments.

Promisingly, addition of these compounds does not appear to affect fermentation, leaving the door wide open for further investigation. We hope to soon share with you more about our research into what could be the next uniquely New Zealand product!

References

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(2) Santel, T.; Pflug, G.; Hemdan, N. Y. A.; Schäfer, A.; Hollenbach, M.; Buchold, M.; Hintersdorf, A.; Lindner, I.; Otto, A.; Bigl, M.; Oerlecke, I.; Hutschenreuter, A.; Sack, U.; Huse, K.; Groth, M.; Birkemeyer, C.; Schellenberger, W.; Gebhardt, R.; Platzer, M.; Weiss, T.; Vijayalakshmi, M. A.; Krüger, M.; Birkenmeier, G. Curcumin Inhibits Glyoxalase 1—A Possible Link to Its Anti-Inflammatory and Anti-Tumor Activity. PLoS ONE 2008, 3 (10), e3508. https://doi.org/10.1371/journal.pone.0003508.
(3) Frickel, E.-M.; Jemth, P.; Widersten, M.; Mannervik, B. Yeast Glyoxalase I Is a Monomeric Enzyme with Two Active Sites *. Journal of Biological Chemistry 2001, 276 (3), 1845–1849. https://doi.org/10.1074/jbc.M005760200