

# Metallo-enzymes for production of nootkatol a potential new citrus flavour

*“The project worked a lot better than even we expected. This BIV research program contributed to the scale-up and commercialisation of nootkatone (grapefruit flavour) production”. [Oxford Biotrans Ltd](#)*



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**OUTCOMES:** Samples of the pure nootkatol isomers were produced and delivered to the industry partner. The potential market of these novel flavours is being assessed. Enzyme variants that gave increased proportions of either nootkatol isomer were generated. Process optimisation also led to improved yields of the nootkatone production process. New strains from the NIBB MiB network can be applied to the systems and processes developed in this BiV project to benefit the UK industrial biotechnology sector.

**INITIAL AIMS:** The sought-after grapefruit flavour compound nootkatone is biosynthesised by air oxidation of valencene catalysed by a haem enzyme, firstly to nootkatol and then nootkatone. Haem enzymes are involved in the biosynthesis of numerous natural products, including flavours such as menthol and nootkatone but also medicinal compounds such as antibiotics, the antimalarial artemisinin and the anticancer drug taxol. The industry partner is developing commercial scale biocatalytic synthesis of nootkatone from valencene. The academic partner will modify the haem enzyme used in this process to produce nootkatol, which is found in minute quantities in grapefruit, to explore its potential as a novel flavour. This primer-project and the nootkatone process will underpin future collaborative work within the metals-in-biology community (1) to test strains optimised (by others) in haem production to further enhance nootkatone/nootkatol synthesis, (2) to manipulate the primary and secondary coordination sphere of the haem moiety to further enhance nootkatol synthesis.

- Nootkatol and nootkatone produced
- Products introduced in Europe & Asia
- Relevant to GCRF-related initiatives on antimicrobial natural products