Drug delivery technology enhances absorption of widely used opioid replacement therapy

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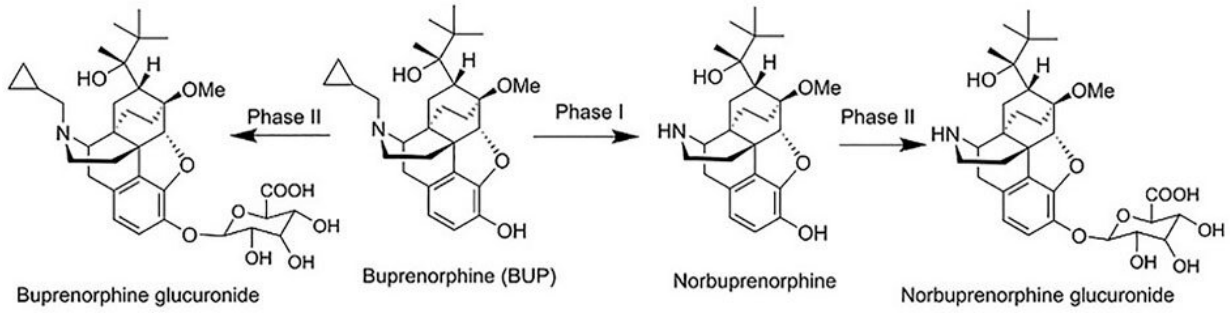

The main metabolism pathway and metabolites of BUP, including norbuprenorphine, norbuprenorphine glucuronide, and buprenorphine glucuronide. Credit: *Frontiers in Pharmacology* (2022). DOI: 10.3389/fphar.2022.879660

Monash University researchers have harnessed a new drug delivery technology to allow the oral administration of buprenorphine (BUP), a drug used for severe pain management and opioid replacement therapy. At present BUP cannot be administered in a formulation such as a capsule that is swallowed.

The team of researchers, led by Director of the Monash Institute of Pharmaceutical Sciences (MIPS) Professor Chris Porter, have today published preclinical proof-of-concept demonstrating that PureTech's

GlyphTM prodrug technology platform has the ability to increase absorption of BUP up to 20-fold, along with statistically significant increases in lymphatic transport.

GlyphTM is specifically designed to enable the trafficking of small molecule drugs directly into the mesenteric lymphatic system following oral administration.

The paper, published in *Frontiers in Pharmacology*, is an exciting step towards enabling patients to more conveniently access an oral BUP product to help manage their pain and/or opioid dependence.

"The ability to develop an oral buprenorphine product with good oral absorption properties could address a range of important unmet clinical needs," said Professor Porter.

"At the moment, the therapeutic potential of buprenorphine is limited by a lack of systemic exposure after the administration of a capsule formulation that can be swallowed. This technology makes that possible. The use of a modified (prodrug) form of the drug that must be processed by the body to release the active form, in combination with a lipid capsule that is not easily dissolved to allow injection, may also help combat diversion of buprenorphine to illicit use."

GlyphTM generates novel orally dosed prodrugs by reversibly linking small molecule drugs to dietary fat molecules. This linkage is designed to channel the drugs directly into the systemic circulation via the lymphatic system, thereby bypassing first-pass liver metabolism which degrades drugs such as BUP and reduces their systemic exposure.

"The research serves as another proof-of-concept for our GlyphTM platform and illustrates how this novel drug delivery technology can be applied to a range of diseases," said Joseph Bolen, Ph.D., chief scientific

officer of PureTech.

"This latest research reinforces our commitment to leveraging validated biology to accelerate the development of the GlyphTM portfolio to improve the oral bioavailability and/or lymphatic targeting of proven drugs."

More information: Tim Quach et al, Triglyceride-Mimetic Prodrugs of Buprenorphine Enhance Oral Bioavailability via Promotion of Lymphatic Transport, *Frontiers in Pharmacology* (2022). DOI: 10.3389/fphar.2022.879660

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