Improve Solubility via Glycosylation

Introduction

Whereas hydroxylation, methylation, fluorination etc. are in the mainstream of medicinal chemistry and ADMET thinking, attaching carbohydrates to improve molecules is considered rather more exotic or not at all (despite an abundance of examples of natural molecules that gain, alter or lose activity by glycosylation or de-glycosylation).

Even if this is considered, glycoside chemistry is difficult. Chemical glycosylation is not in itself straightforward, and since many interesting molecules have more than one or even many “glycosylatable” side groups (-OH, -COOH, -NH, -SH), all the other groups but the one in question need to be chemically blocked, a very tedious process.

Using small molecule glycosyl-transferase enzymes almost any given molecule (with appropriate side groups) can be glycosylated, most often regio-specifically (thus abolishing the need for side group blocking), in many cases even stereo-specifically and, if needed, with a number of different sugars (glucose, galactose, xylose, glucuronic acid, rhamnose etc.).

Cadalene

Lee et al. demonstrated that glycosylated cadalene derivatives were potentially superior prodrugs by improving solubility and therapeutic efficacy. In vitro cell viability assays confirmed that glycosylated cadalenes were less toxic and more soluble than cadalene itself, and oral administration to mice with xenografted tumours strongly indicated superior therapeutic efficacy, likely due to better uptake of the molecule by the tumour cells.
https://www.sciencedirect.com/science/article/pii/S0960894X07010281?via%3Dihub

Curcumin

Kaminaga et al. showed that *Catharanthus roseus* cell suspension cultures converted curcumin into a series of glucosides with enhanced water solubility. It was found that water solubility of curcumin monoglucoside was increased to 7.0 nmol/ml, which was 230-fold higher than that of curcumin (30 pmol/ml). The solubility increased about 20 million-fold in the case of curcumin digentiobioside (4 glucose - 650 µmol/ml) compared with the solubility of curcumin.
https://febs.onlinelibrary.wiley.com/doi/full/10.1016/S0014-5793%2803%2901265-1

Glycosylation provides remarkable opportunities for improving characteristics, use and production of small molecules that are not currently being taken advantage of. River Stone has significant proprietary knowledge as well as a collection of diverse enzymes that have the potential to help our customers doing just that.

What is the Gly-it platform?

The Gly-it platform is a library of 380 diverse “Family 1” UDP-glucose dependent glycosyltransferase enzymes (UGTs) plus associated screening, analytical and lab scale production protocols (“Family 1” denotes glycosyltransferases that will glycosylate small molecules).

All the enzymes in Gly-it are found in plants (which have diverse UGTs to work with the diverse range of small molecules that occur in plants or their environment). The kit contains enzymes from all known Family 1 UGT sub-families and sub-sub-families and from a wide set of evolutionarily diverse plants.

The majority of the enzymes will be able to add glucose to small molecule substrates with relevant functional groups. Some enzymes will work with other sugars (such as xylose, rhamnose, galactose or glucuronic acid). We can advise you on the best path for specific sugars.

We realize that this may be your first step in determining if Gly-it technology will be able to help you in your current project. We are happy to assist you in determining if Gly-It is the right fit.

To discuss, or for more help, just get in touch.
We would like to make sure Gly-it is a proper fit for your current goals.

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