

# Furfural a key model inhibitor in the development of lignocellulosic hydrolysate strains

## Background

- Dilute acid pretreatment of biomass at high temperature and pressure is commonly utilized to efficiently solubilize the pentose fraction by hydrolyzing the hemicellulose fibers and releasing lignin; the process results in formation of furans – furfural and 5-hydroxymethyl furfural – and other inhibitors which are detrimental to microbial metabolism. It is important to develop inhibitor tolerant microbial strains which can convert lignocellulosic carbon into an industrial metabolite of interest with high yield and productivity.

## Approach

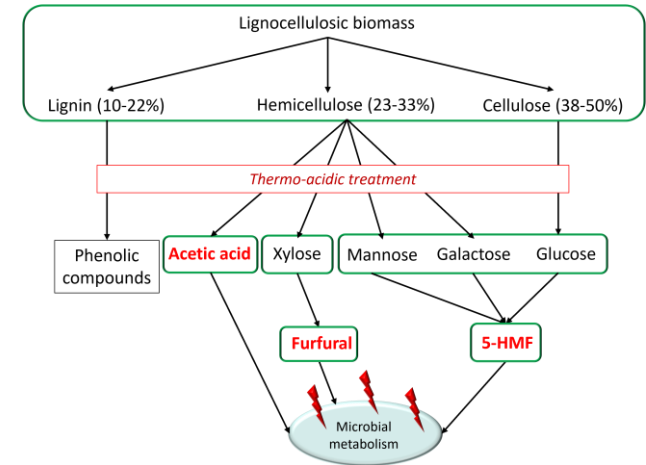
- A literature search was performed for furan inhibitors – furfural and 5-hydroxymethyl furfural – and their role in bioenergy research involving microbial catalysts. A diverse families of genes, from multiple microbes, are reported in this review as involved in conferring tolerance against both furfural and 5-hydroxymethyl furfural.

## Results

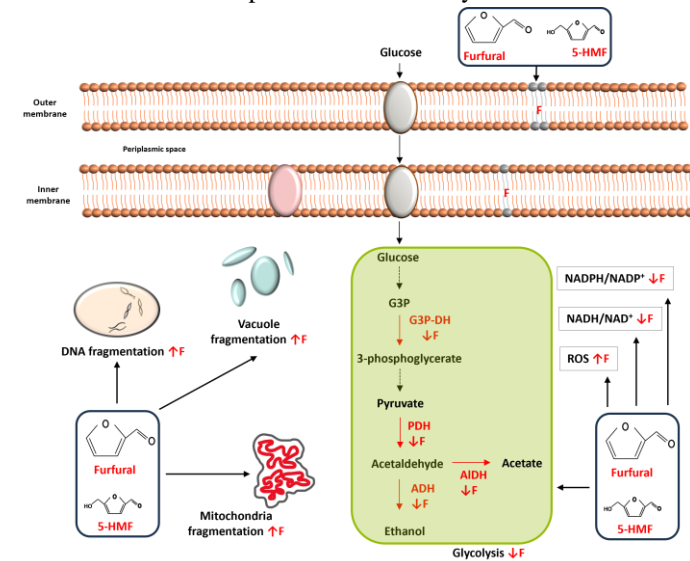
- Furfural is relatively more toxic to microbial metabolism as compared to 5-hydroxymethyl furfural.
- Furfural results in lowering of cellular NADPH levels and leads to an arrest in microbial growth.
- Genes from oxidoreductase families (e.g., overexpression NADPH specific protein encoding genes) are the most widely reportedly involved in conferring tolerance.
- There are many shared targets from furfural with acetic acid tolerance.
- Overexpression of genes involved in membrane, polyamine and pyrimidine biosynthesis, and sulfur assimilation are reported to be beneficial in conferring tolerance.
- Overexpression of ABC-type transporters and transcription factors is also beneficial in conferring tolerance.

## Significance

- Furfural has potential to be used as a model inhibitor in the development of robust strains that can tolerate stressful conditions encountered in using lignocellulosic hydrolysate.
- Furfural tolerant strains can serve as a microbial chassis to produce a variety of compounds of industrial importance using the cheap lignocellulosic hydrolysate as a carbon source.



Components of lignocellulosic biomass and products generated in thermo-acidic pretreatment. The proportions vary with the pretreatment severity.



Reported cellular targets of furfural inhibition. Furfural targets highlighted in red.

Jilani SB and Olson DG. Microbial Cell Factories (2023) 22, 221. doi.org/10.1186/s12934-023-02223-x