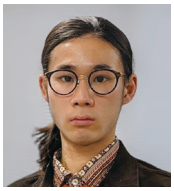
Biomanufacturing using abiotically synthesized non-natural sugars

Research Center for Solar Energy Chemistry, Graduate School of Engineering Science

Professor Shuji Nakanishi Researchmap https://researchmap.jp/read0191166?lang=en

Specially Appointed Researcher Hiro Tabata Researchmap https://researchmap.jp/tbt?lang=en



Abstract

Biomass sugars like glucose and fructose are crucial both as resources for human food production and as substrates for bio-manufacturing. Our research group has found that oxometalates, such as sodium tungstate, can act as catalysts for sugar synthesis under neutral conditions. This reaction yields non-natural sugars—sugars not typically found in nature—and we have demonstrated that these abiotically synthesized non-natural sugars are metabolizable by microorganisms. Using Corynebacterium as a model organism, we successfully produced lactic acid through fermentation with abiotically synthesized non-natural sugars as the sole substrate.

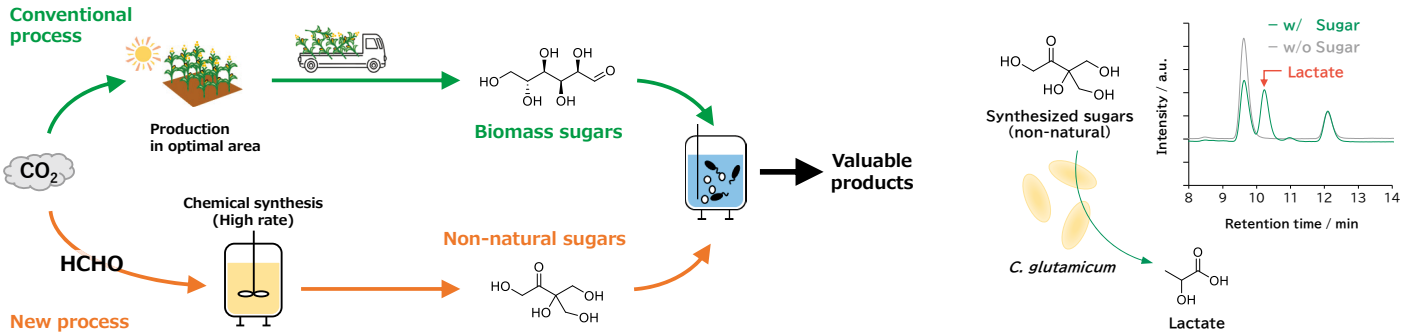
Background & Results

This study marks the world's first successful example of biomanufacturing using abiotically synthesized non-natural sugars as a raw material. The chemical synthesis of these non-natural sugars is at least several hundred times faster than photosynthesis, requiring minimal water and nutrients, thereby enabling the sustainable production of sugars without competing with food resources. In the future, this technology could emerge as a novel sugar resource, capable of replacing natural sugars like glucose. It has the potential to evolve into a 'high-speed, on-site sugar production system,' converting CO_2 into metabolizable sugars for organisms. This breakthrough is expected to significantly advance environmentally friendly bio-manufacturing technologies.

Significance of the research and Future perspective

Biomass sugars, such as glucose and fructose, are fundamental to human food production and serve as substrates for bio-manufacturing technologies. These sugars are derived through photosynthesis, using water and CO_2 as raw materials. However, large-scale biomass sugar production through photosynthesis demands substantial water, nutrient salts, and extensive land areas, which raises sustainability concerns within planetary boundaries. Furthermore, biomass sugars face supply limitations that could lead to competition with food resources due to the increasing demand for fuels and chemicals.

Chemical synthesis of sugars involves two main steps: (1) the formation of formaldehyde (HCHO) via CO_2 reduction and (2) subsequent sugar synthesis through the formose reaction, using HCHO as a substrate. A major challenge in this process has been developing catalysts that selectively promote sugar synthesis within the formose reaction. As this reaction takes place in an alkaline environment prone to numerous side reactions, achieving high sugar yield has been challenging. However, our research group developed a catalyst that enables highly selective sugar synthesis under neutral conditions, resulting in an improvement in sugar yield. Notably, despite the abiotically synthesized sugars having non-natural structures, they are metabolizable by microorganisms. Using Corynebacterium as a model organism, we identified growth inhibitors within the synthetic sugar solution and successfully produced lactic acid with synthetic sugars as the sole substrate. This accomplishment represents the first instance globally of bio-manufacturing using catalytically synthesized non-natural sugars as substrates.



Patent	PCT/JP2022/038093, PCT/JP2024/031084, PCT/JP/2024/029914
Treatise	Tabata, Hiro; Chikatani, Genta; Nishijima, Hiroaki et al. Construction of an autocatalytic reaction cycle in neutral medium for synthesis of life-sustaining sugars. Chemical Science. 2023, 14, 13475-13484. doi: 10.1039/D3SC03377E Tabata, Hiro; Nishijima, Hiroaki; Yamada, Yuki et al. Microbial biomanufacturing using chemically synthesized non-natural sugars as the substrate. ChemBioChem. 2024, 25(2), e202300760. doi: 10.1002/cbic.202300760
URL	https://resou.osaka-u.ac.jp/en/research/2024/20240208_1
Keyword	biomanufacturing, CO_2 utilization, sugars