Supplemental material for Frontiers in Microbiology

**Fig. S1** NMR spectrum of DNJ. (**A**), DNJ synthesized with unlabeled glucose as precursor; (**B**), DNJ synthesized with labeled 1-13C-glucose as precursor; (**C**), DNJ synthesized with labeled 2-13C-glucose as precursor

**Fig. S2** Time course curves of DNJ content, biomass of UN-8, residual glucose under the optimized fermentation strategy

**Fig. S3** The chemical structures ofmannose, sorbose, mannitol, sorbitol, rhamnose

**Table S1**. Different regulation strategies of adding metabolism inhibitors, precursor and intermediate analogs on the production of DNJ

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| --- | --- | --- | --- | --- |
| Regulation strategies | Compounds | Concentrations | Time | Target enzyme |
| Mevalonate pathway inhibitor | simvastatin | 0.15-0.75 mM | 0 h, 24 h | HMGR (Buhaescu and Izzedine, 2007) |
| Shikimate pathway inhibitor | EDTA | 3-12 mM | 0 h, 24 h | DHQS, SK (Sun et al., 2009) |
| EMP inhibitors | iodoacetic acid | 12.5-125 mg/L | 0 h, 18 h, 24 h | GAPDH (Wang et al., 2002) |
| sodium citrate | 2-8 g/L | 0 h | PFK, PK (Liu et al., 2004) |
| HMP inhibitor | sodium phosphate | 0.1-0.4 g/L | 24 h | G6PD (Yu and Pan, 1996) |
| TCA inhibitor | sodium malonate | 1-5 g/L | 24 h | SDH (Zeng et al., 2019) |
| Precursor and intermediate analogs | mannitol, sorbitol, rhamnose, mannose, sorbose | 1-4 g/L | 0 h |  |
| Precursor | glucose | 0.5-8 g/L | 24 h |  |

HMGR, 3-Hydroxy-3-methylglutaryl-CoA reductase; DHQS, 3-Dehydroquinate synthase; SK, shikimate kinase;

GAPDH, glyceraldehyde-3-phosphate dehydrogenase; PFK, phosphofructokinase; PK, pyruvate kinase

G6PD, Glucose-6-phosphate dehydrogenase; SDH, succinodehydrogenase;

**Table S2**. Factors and levels for the orthogonal test in 250 ml shake flask

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | level | | |
| 1 | 2 | 3 |
| A, Concentration of glucose supplementation (g) | 0.250 | 0.300 | 0.350 |
| B, Time of glucose supplementation (h) | 24 | 26 | 28 |
| C, Concentration of sorbose (g) | 0.050 | 0.075 | 0.100 |
| D, Time of iodoacetic acid supplementation (h) | 16 | 18 | 20 |
| E, Error |  |  |  |