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Towards sustainable feedstocks: A guide to electron donors for microbial carbon fixation

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The replacement of fossil and agricultural feedstocks with sustainable alternatives for the production of chemicals and fuels is a societal and environmental necessity. This challenge can be tackled by using inorganic or one-carbon compounds as electron donors for microbial CO_2 fixation and bioproduction. Yet, considering the wide array of microbial electron donors, which are the best suited for bioindustry? Here, we propose criteria to evaluate these compounds, considering factors such as production methods, physicochemical properties, and microbial utilization. H_2, CO, and formate emerge as the most promising electron donors as they can be produced electrochemically at high efficiency and, importantly, have reduction potentials low enough to directly reduce the cellular electron carriers. Still, further research towards the production and utilization of other electron donors — especially phosphite — might unlock the full potential of microbial CO_2 fixation and bioproduction.

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Introduction

One of the grand challenges of our times is replacing fossil-based production of chemicals and fuels by sustainable alternatives with a lower carbon footprint. While agricultural resources are being pursued as such feedstocks, the industrial utilization of most of them — i.e., sugar, starch, and oil — directly competes with food and feed production. The use of lignocellulosic biomass as an alternative feedstock that does not undermine food security is constrained by limited availability and inefficient processing. Furthermore, plant-based feedstocks are fundamentally limited by the low efficiency of biological photosynthesis [1]. This is also a major barrier for the use of cyanobacteria and algae as cell factories [2] in addition to the high cost of photobioreactor systems and the limited genetic toolboxes for their engineering [3,4].

As an alternative, a promising bioproduction strategy is the use of reduced inorganic or one-carbon (C1) electron donors to support microbial CO_2 fixation. These compounds can be sustainably obtained from waste streams or readily regenerated by the use of unlimited resources, such as light, water, and CO_2. The electron donors can then provide reducing power and energy to drive CO_2 fixation in chemolithoautotrophic or methylotrophic microorganisms (for methylotrophs see also review [5,6•,7••]. Engineering these microorganisms for the production of chemicals can therefore provide a sustainable and efficient production chain with minimal carbon footprint. However, given the wide array of microbial electron donors, it is an open question which donors are most suitable to serve as feedstocks for biotechnological production.

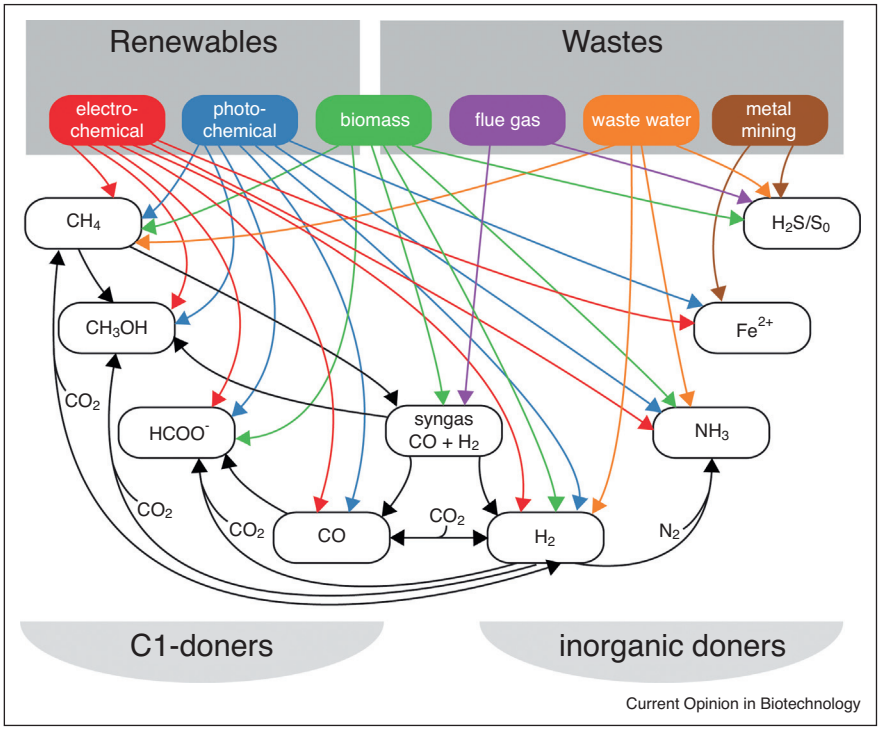
This review addresses this question by putting forward practical guidelines by which electron donors should be evaluated and compared. Using these guidelines, we systematically assess different electron donors to uncover their advantages and drawbacks for supporting microbial bioproduction. We note that C1-compounds may not only serve as electron donors for CO_2 fixation but can also be assimilated directly; however, we do not elaborate on this option and instead refer the reader to recent reviews on C1-assimilation pathways [8–10].

Guidelines for assessing the biotechnological suitability of electron donors

(1) Abundant, sustainable sources

Microbial electron donors can be sustainably obtained by two general approaches (Figure 1): (i) extraction from waste streams — mostly industrial flue gas, waste water, and mining residues — and (ii) production or regeneration via renewable energy sources. The first provides readily available, low-cost feedstocks, but has a limited potential to satisfy the global demand of fuels and chemical compounds. The second approach is especially promising, as it could depend on sources with an almost

Figure 1



Renewable and waste sources for different electron donors. References on sources and production processes are available in Supplementary Table 1.

unlimited supply such as renewably produced electricity — e.g. from solar, wind, or hydro — or light supporting direct photochemical conversions. The source of electrons in these cases is ultimately water, and the source of carbon is ultimately CO_2, both abundantly available. We note that for most biotechnological applications, concentrated CO_2 will be required, which in the short term can be derived from industrial flue gas. However, for future large-scale applications, CO_2 will need to be captured and concentrated from air, a process that still requires much optimization and is intensively researched [11].

By oxidizing water, electrochemical systems can generate a variety of reduced feedstocks (Figure 1) [12••,13]. The performance of such systems can be evaluated by their: (i) Faraday efficiency — percentage of electrons going to a desired reduced product; (ii) energetic efficiency — fraction of energy conserved in the desired product; (iii) current density — formation rate of the desired product; (iv) electrode composition — minimizing use of metal catalysts; (v) durability — maximizing lifetime of the system [12••]. These parameters vary widely for the production of different donors, which strongly affect their feasibility as biotechnological feedstocks. As an alternative, several microbial feedstocks can be produced photochemically (Figure 1), where light is directly absorbed by chemical catalysts to oxidize water and regenerate the donors [14]. However, this technology is not as mature as electrochemical production, for which the obtained efficiencies and rates are currently much higher [13,14].

In addition, biomass, either produced with the purpose of serving as feedstock or as a waste residue, can serve to efficiently produce reduced donors, e.g. via gasification [15•] or partial oxidation [16•] (Figure 1). While several donors can be obtained from natural gas or other fossil carbons, these unsustainable resources are not considered here.

(2) Low reduction potential

An electron donor should preferably have a reduction potential low enough to directly reduce the cellular redox carriers. While multiple such carriers play a role in different organisms — e.g. ferredoxin, FAD, FMN, quinones, cytochromes or F420 — the dominant carrier, also for CO_2 fixation, is NAD(P)H. The standard reduction potential of $NAD(P)^+$/NAD(P)H is −320 mV, and its physiological potential lies between −370 and −250 mV, depending on the cellular ratio between the reduced and oxidized species. Hence, ideally, an electron donor should have a standard potential of ∼−400 mV or below. If an electron donor with a higher potential is used (e.g. Fe^{2+} and NH_3), reverse electron flow is required to reduce $NAD(P)^+$. In this process, the cellular proton