Prospective CO_2 and CO bioconversion into ectoines using novel microbial platforms

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Abstract

Microbial conversion of CO_2 and CO into chemicals is a promising route that can contribute to the cost-effective reduction of anthropogenic green house and waste gas emissions and create a more circular economy. However, the biotechnological valorization of CO_2 and CO into chemicals is still restricted by the limited number of model microorganisms implemented, and the small profit margin of the products synthesized. This perspective paper intends to explore the genetic potential for the microbial conversion of CO_2 and CO into ectoines, in a tentative to broaden bioconversion platforms and the portfolio of products from C_1 gas fermentations. Ectoine and hydroxyectoine can be produced by microorganisms growing at high salinity. They are high-value commodities for the pharmaceutical and medical sectors (1000-1200 €/kg). Currently microbial ectoine production is based on sugar fermentations, but expansion to other more sustainable and cheaper substrates is desirable. In this work, a literature review to identify halophilic microbes able to use CO_2 and CO as a carbon source was performed. Subsequently, genomes of this poll of microbes were mined for genes that encode for ectoine and hydroxyectoine synthesis (*ectABCD, ask*, *asd* and *ask_ect*). As a result, we identified a total of 31 species with the genetic potential to synthesize ectoine and 14 to synthesize hydroxyectoine. These microbes represent the basis for the creation of novel microbial-platforms that can promote the development of cost-effective and sustainable valorization chains of CO_2 and CO in different industrial scenarios.

Keywords: valuable compounds, greenhouse gases, bioconversion, gas fermentation, circular economy.

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Introduction

A primary target of a profitable circular economy is the development of new bio-production systems capable of recycling and creating value out of greenhouse gases and industrial off-gas emissions (European commission 2018). The current chemical market is worth more than 3.6 trillion € per year globally, but less than 5% of the chemicals are produced using biotechnological processes. Most of the existing biotechnologies use sugars as feedstock, whose price accounts for up to 50% of the production costs (Zeng 2019). Besides, utilization of sugars for the production of chemicals directly competes with food markets and is environmentally unsustainable (Ritala et al. 2017). In recent years, the microbial conversion of point source CO_2 and CO emissions have received great attention as an alternative to sugar fermentations (Nisar et al. 2021; Kumar et al. 2022). The availability of these gases is practically unlimited, flue gases are practically free, and the valorization of CO_2 and CO acts as an atmospheric pollution and climate change mitigation strategy (Metz et al. 2018). However, despite the potential for sustainable production of added-value compounds from CO_2 and CO, current physico-chemical and biological technologies are seldomly cost-effective. Physico-chemical transformation of CO_2 into industrial compounds of interest is difficult because it requires high energy input as a result of the oxidized low-energy carbon of the CO_2 molecule (Gabrielli et al. 2020). For biological CO_2 transformation, photobioreactors are the most studied and developed biological technologies (Anand et al. 2020). However, photosynthesis has a relatively low energy efficiency (less than 3%). Open systems have limitations such as uneven light intensity, evaporative losses, diffusion of CO_2 to the atmosphere, undesired contamination and a larger footprint. Closed photobioreactors are expensive and often require nitrogen dosing to improve productivity (Zeng 2019; Bose et al. 2019). CO, instead, is a high-energy molecule and can be converted using chemical synthesis. Nevertheless, chemical catalysis usually requires energy-intensive conditions (e.g. Fischer-Tropsch process), a fixed H_2 to CO ratio, and costly removal of syngas impurities to avoid catalyst poisoning (Cordero et al. 2019).

CO_2 and CO can be converted using chemolithoautotrophic microorganisms in a process independent from light, known as dark carbon fixation. Chemolithoautotrophic organisms obtain their energy from redox reactions and their carbon from CO_2 fixation or/and CO. Technologically, dark carbon fixation can be a cost-effective option to transform CO_2 and CO emissions into chemical building blocks (Claassens et al. 2018). Promising cell factories are researched for the production of plastics, diesels, single cell protein and extracellular polysaccharides. Table 1 shows an overview of chemicals produced from CO_2 and CO (complete review of microbial compounds produced from CO_2 and CO, yields and references in supplementary information 1, Table S1). However, current processes apply a restricted number of model microorganisms, such as acetogens, with a small portfolio of products, mainly alcohols and organic acids (Zeng 2019). Consequently, the development of new biotechnologies that expand microbial catalysts used for transforming CO_2 and CO and their product portfolio is of great interest for the transition pathway to a fossil-free circular economy.

Table 1: Examples of microbial compounds currently produced from CO_2 and CO				
Products	**Microorganisms**		**Carbon source**	**Energy source**
	Pure culture	***Co-culture***		
Alcohols				
Ethanol Butanol Hexanol Isopropanol	• *C. butyricum* • *C. aceticum* • *C. carboxidivorans* • *C. ljungdahlii*	• *C. autoethanogenum & C. kluyveri* • *C. ljungdahlii & C. kluyveri* • Mixed culture dominated by *Acetobacterium & Clostridium* species	CO, CO_2	H_2, CO
Biodiesel				
FAMEs (C_{11}–C_{24}) Triacylglycerides (C_{16}-C_{18})	• *Bacillus cereus* • *Halomonas stevensii* • *Pseudomonas aeruginosa*	• *Moorella thermoacetica & Yarrowia lipolytica*	CO_2	Fe[II], NaS_2O_3, H_2
Organic Acids				
Acetate Butyrate Caproate Formate Glutamate Hydroxypropionate Malate Methylenesuccinate	• *Acetobacterium woodi* • *C. ljungdahlii* • *Sulfurovum lithotrophicum*	• *C. autoethanogenum & C. kluyveri* • *C. aceticum & C. kluyveri* • *Eubacterium limosum & E. coli* • *C. ljungdahlii & Aspergillus oryzae*	CO, CO_2	H_2, CO
Bioplastics				
PHA PHB	• *Cupriavidus eutrophus* • *C. coskatii* • *Cupriavidus necator* • *Ideonella dechloratanus* • *Ralstonia eutropha* • *Rhodospirillum rubrum*		CO, CO_2	H_2, CO
Extracellular polysaccharides and secondary carboxy-driven bioproducts				
EPS	• *Serratia sp. ISTD04*		CO_2[a]	
Heptadecane		• *Acetobacterium woodii & Acinetobacter baylyi*	CO_2	H_2
Long alkyl esters		• *Sporomusa ovata & Acinetobacter baylyi*	CO_2	electricity
Microbial protein	• *Cupriavidus necator*	• *C. ljungdahlii & Saccharomyces cerevisiae*	CO_2	H_2
Sesquiterpene (E)-α-bisabolene	• *Hydrogenophaga pseudoflava*		CO, CO_2	H_2, CO

[a] Supplementation with glucose. **C.**: *Clostridium*, **FAME:** fatty acids methyl esters, **PHA:** Polyhydroxyalkanoates, **PHB**: poly-3-hydroxybutyrate, **EPS:** Extracellular polymeric substance.

High-value compounds produced by microbes at high salinities: Ectoine and Hydroxyectoine

Microorganisms growing in high-salinity environments produce organic osmolytes (also known as extremolytes) to protect cell integrity and ensure survival (Czech et al. 2018a). Industry has spotlighted extremolytes formed at high salinity as an 'unexploited gold-mine' with opportunities for the cosmetic, medical, and food industries (Becker and Wittmann 2020). Out of all the extremolytes, ectoines (ectoine and its hydroxyectoine derivative) are highly interesting as they provide protection against an array of stress factors (e.g. salinity, desiccation, oxygen radicals, temperature, UV light) which makes of them multi-functional agents of great market value (Becker and Wittmann 2020; Liu et al. 2021).

Ectoine is a cyclic imino-acid (2-methyl-1,4,5,6-tetrahydropyrimidine-4-carboxylic acid) which molecular structure enhances hydrogen bonding in aqueous solution (Czech et al. 2018a). This allows ectoine to bind water and form an ectoine-hydro-complex that acts as a protective hydro-layer on cell surfaces and macromolecules. This makes ectoine a highly effective stabilizer of proteins, DNA–protein complexes, nucleic acids, cell membranes and tissues (Figure 1). Current ectoine retail value is of approximately 1000 € kg^{-1} and market trends indicate that ectoine's importance in the chemical industry will continue to grow inferred from its novel commercial products (Liu et al. 2021). Bitop AG manufactures 90% of the current market needs (data 2016), but other companies such as Bloomage Biotechnology Corporation are starting to produce ectoine industrially (Becker and Wittmann 2020). The primary application is the cosmetic industry: mainly for skin and hair care products (industrial producers: Bitop AG, DADO-cosmed GmbH, Börlind Gesellschaft für, Jan Dekker). There is also expansion towards the medical industry due to ectoines anti-allergenic and anti-desiccant properties. Companies like Johnson & Johnson, Pari GmbH, and Bitop AG are already incorporating ectoine in nasal sprays, eye drops, mouth and throat spray, anti-dermatitis creams and lung inhalation fluids (Becker and Wittmann 2020).

Although the pathway for ectoine production can vary slightly from one organism to another, it involves three specific enzymes encoded by the conserved gene cluster *ectABC* (Figure 1): l-2,4-diaminobutyric acid (DABA) transaminase (EctB), DABA acetyltransferase (EctA) and ectoine synthase (EctC). EctC is considered a marker protein for ectoine producers (Czech et al. 2019). Sometimes an additional gene of aspartokinase (*ask_ect*) and/or the gene (*ectR*) for a MarR-type regulator are observed within the *ectABC* cluster (Czech et al. 2018a).

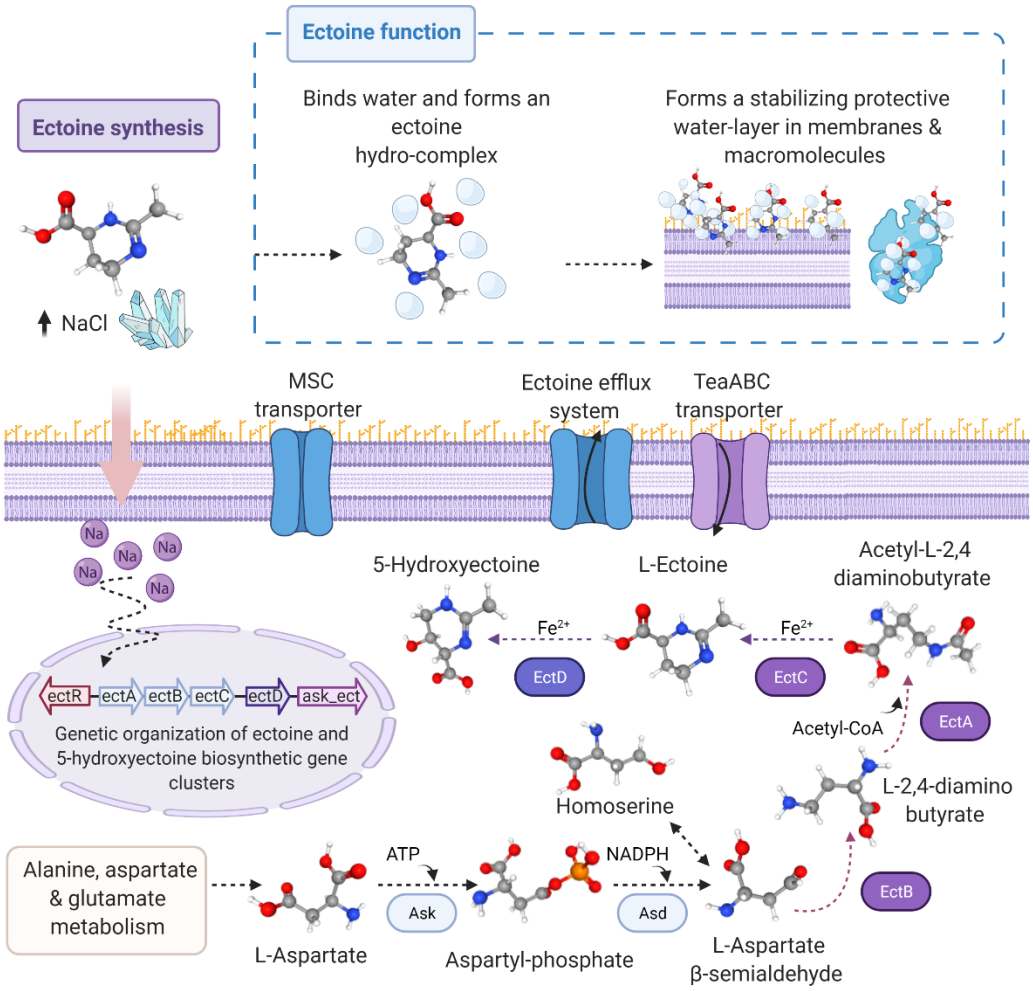

Figure 1. Gene cluster for ectoine and hydroxyectoine production in *Acidiphilum cryptum* and general microbial biosynthetic pathway for ectoine and hydroxyectoine production in the cell. *ectR* encodes a MarR-type regulator; *ectA*, the protein diaminobutyric acid (DABA) acetyltransferase (EctA); *ectB*, DABA aminotransferase (EctB); *ectC*, ectoine synthase (EctC); *ectD*, ectoine hydroxylase (EctD); *ask_ect*, a specialized aspartokinase (Ask); Asd stands for l-aspartate-semialdehyde-dehydrogenase. Dotted box with possible mechanisms for ectoine protection in the cells.

Members of *Halomonas*, *Brevibacterium* and *Chromohalobacter* genera can naturally accumulate high concentrations of ectoine (15% cdw) when cultured at high salinity with simple sugars and yeast extract. *Halomonas elongata* is the most widely used strain for industrial ectoine production. Bitop AG uses non-genetically modified *'superleaky'* mutants of *H. elongata* to produce tons of ectoines yearly (Kunte et al. 2014; Becker and Wittmann 2020). These mutants excrete ectoine to the medium avoiding the need for hiper and hipo osmotic shocks to recover intra-cellular ectoine from the biomass (bio-milking process). Besides this advantage, the process with '*superleaky*' strains is still costly due the high amounts of glucose and oxygen required, and

the corrosive characteristics of the high salinity medium (Kunte et al. 2014; Liu et al. 2021). Recent research and commercial attempts have focused on cost-effective biotechnology aimed at synthesizing ectoine at lower salinities using engineered microorganisms, however, the preference of using natural non-GMO extremolytes by the cosmetic market calls for other alternative processes (Becker and Wittmann 2020). Table 2 shows some of the high-yield ectoine producers (complete overview of ectoine producers can be found in supplementary information 1, Table S2) .

Table 2: Most promising implemented microorganisms for ectoine production

Microorganism	Substrate	Production yield (mg g_{dcw}^{-1})	NaCl (M)	Condition	Ref.
Non-genetically modified halophilic ectoine producers					
Brevibacterium epidermis DSM 20659	Sodium glutamate & yeast extract	160	1	Aerobic batch fermentation (pH=7, 30°C)	(Onraedt et al. 2005)
Chromohalobacter salexigens DSM3043	Glucose	540	1.8	Aerobic continuous bioreactor (pH=7.5, 37°C)	(Fallet et al. 2010)
Halomonas elongata DSM2581	Glucose	1365[a]	2.6	Aerobic batch fermentation (pH=7.2, 37°C)	(Fatollahi et al. 2021)
Halomonas salina DSM5928	Sodium glutamate	358	0.5[b]	Aerobic batch fermentation (pH=7.2, 30°C)	(Zhang et al. 2009)
	Genetically modified halophilic ectoine producers				
Halomonas bluephagenesis TD-ADEL-58	Sodium aspartate, citrate & glucose	1120[a]	1	Aerobic fed-batch fermentation (pH=~9, 37°C)	(Ma et al. 2020)
Halomonas hydrothermalis Y2	Monosodium glutamate	765	1.1	Aerobic fed-batch fermentation (pH=9, 30°C)	(Zhao et al. 2019)
	Genetically modified non-natural ectoine producers				
Corynebacterium glutamicum Ecto5	Glucose	1800[a]	0.01	Aerobic fed-batch fermentation	(Pérez-García et al. 2017)
E. coli BW25113 (*pBAD-ectABC*)	Aspartate, glycerol and glucose	4048[a]	0.5	Aerobic fed-batch fermentation (pH=7, 30°C)	(He et al. 2015)
E. coli DH5α (pASK_ectABCD$_m$)	Glycerol	2900[a]	0.01	Aerobic batch (pH=7, 37°C)	(Bethlehem and Moritz 2020)
E. coli SK51 (pLC75)	Glucose	1000[a]	0.4	Aerobic batch (37°C)	(Czech et al. 2018b)

[a]Excreted to the medium. [b]Phosphate, citrate and sulfate salts were also included.

A compatible solute derived from ectoine that has recently received commercial attention is hydroxyectoine (5-hydroxy-2-methyl-1,4,5,6-tetrahydropyrimidine-4-carboxylic acid) (Czech et al. 2019). Hydroxyectoine is produced by a substantial amount of ectoine producers through a position- and stereo-specific hydroxylation

121 catalyzed by an ectoine hydroxylase (EctD) (Czech et al. 2018a). Compared to ectoine, hydroxyectoine confers
122 additional protective properties due to its hydroxylated nature and has a higher price (1200 € kg^{-1}) (Becker and
123 Wittmann 2020). Hydroxyectoine plays an important role in heat stress protection, increasing the melting
124 temperature of DNA, and confers stronger desiccation resistance due to its ability to form glasses (Liu et al.
125 2019). With the exception of some *Marinococcus* strains and *Pseudomonas stuzeri* (Schiraldi et al. 2006; Seip
126 et al. 2011), hydroxyectoine and ectoine are naturally co-produced. Commercial strains for ectoine production,
127 such as *H. elongata*, can be manipulated to increase its hydroxyectoine content (to a maximum of approximately
128 50%) via desiccation at extreme salinity and elevated temperature. However, growth under extreme conditions
129 and subsequent chromatographic separation procedures increase production costs. Thus, industrial ectoines are
130 usually sold as mixtures of ectoine and hydroxyectoine (Liu et al. 2021).

131 As hydroxyectoine is in high demand due to its superior protective properties, current research has focused on
132 the singular production of this analogue. The highest hydroxyectoine production yields have been obtained in
133 cultivations with natural *Halomonas* species at high salinity. Although some recent research has focused on the
134 genetic modification of non-natural producers with the aim of synthesizing hydroxyectoine as the only osmolite
135 (Table 3; a whole overview of hydroxyectoine producers, conditions, and yields can be found in supplementary
136 information 1, Table S3).

Table 3: Most promising implemented microorganisms for hidroxyectoine production

Microorganism	Substrate	Production yield[a] ($mg\ g_{dcw}^{-1}$)	NaCl (M)	Condition	Ectoine (byproduct)	Ref.
Non-genetically modified natural hidroxiectoine producers						
Halomonas salina BCRC 17875	Sodium glutamate & yeast extract	9830[b]	0.1	Aerobic fed-batch fermentation (pH=7, 30°C)	N.R	(Chen et al. 2019)
Marinococcus sp. M52	Glucose and fish peptone	135	1.7	Aerobic fed-batch fermentation (pH=7.5, 35°C)	N.D	(Frings et al. 1995)
Pseudomonas stutzeri DSM5190T	Glucose	76	0.8	Aerobic batch (pH=7.2, 37°C)	N.D	(Seip et al. 2011)
Genetically modified non-natural hydroxyectoine producers						
E. coli FF4169 (pMP41)	Glucose & ectoine	2.1 ($g\ L^{-1}$)[b]	0.4	Aerobic fed-batch fermentation (pH=7.5, 37°C)	N.D	(Czech et al. 2016)
E. coli DH5α (*pASK_ectABCDask*)	Glycerol	2200[b]	0.5	Aerobic batch (pH=7.5, 37°C)	4 %	(Bethlehem and Moritz 2020)
Hansenula polymorpha (ALU3/EctBACD[h])	Methanol & Sorbitol	57.7	0	Aerobic fed-batch fermentation (pH=7.5, 37°C)	2 %	(Eilert et al. 2013)

137 [a]Values refer exclusively to hydroxyectoine. [b]Excreted to the medium. N.R. Not reported. N.D. Not detected.

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C_1 compounds as alternative feedstock for ectoine and hydroxyectoine production

Although there has been tremendous progress in ectoine and hydroxyectoine biosynthesis, there is little integration of sustainable feedstock and a lack of studies about the use of renewable carbon and energy sources for ectoine production. In this regard, new bioproduction systems using waste C_1 compounds as carbon supply could lower production costs, while mitigating greenhouse gas emissions. Different halotolerant aerobic methanotrophs have been identified as able to accumulate ectoine; most of them belong to the genus *Methylomicrobium*, e.g. *M. alcaliphilum, M. buryatense, M. kenyense* or *M. japanense*, although other bacteria such as, *Methylobacter marinus* and *Methylohalobius cremeensis* are also ectoine producers (Kalyuzhnaya et al. 2008). Out of all, *M. alcaliphilum* is considered the most efficient methanotrophic ectoine producer (achieving ectoine specific yields of 230 ± 20 mg g_{dcw}^{-1}) (Khmelenina et al. 2015). In fact, the process feasibility of *M. alcaliphilum* in bio-reactors has been demonstrated in aerobic fed-batch fermentation, reaching extracellular concentrations of 253.4 ± 55.1 mg L^{-1} ectoine and recoveries of ~ 70% of the total intra-cellular ectoine (Cantera et al. 2017). Further on, the use of consortia has been preferred for the production of ectoine from CH_4 in continuous, due to their higher resilience and two times higher ectoine productivities (Cantera et al. 2020). In fact, a recent techno-Economic and Sensitivity Analysis of the production of ectoine from biogas in waste treatment facilities has demonstrated that the production of ectoine from biogas has high profitability with a net present value evaluated at 20 years (NPV_{20}) of 33.6 M€ (Pérez et al. 2021). Nevertheless, despite the enormous potential of biogas as feedstock for ectoine production, its large-scale production is still constrained by the limitation of CH_4 solubility in liquid medium and gas-liquid mass transfer, eventually resulting in low product titers.

In view of overcoming these rate-limiting factor, a novel approach of using different C_1 gases with greater mass transfer, such as CO_2, and processes that integrate aerobic and anaerobic microbes able to use CO_2 and CO as carbon source could broaden and make more sustainable this bioconversion platform.

Different approaches could be taken for the bio-conversion of CO_2 and CO into ectoines. Synthetic co-cultures formed by mesophilic microorganisms able to produce organic acids or ethanol from CO_2 or CO, such as acetogens, coupled to heterotrophic ectoine producers, such as *Halomonas* species, could be used to enhance the valorization process of these C_1 gases. Nevertheless, two step fermentations would be required for the implementation of this technology by virtue of operational restrictions. These restrictions include the high salinity needed for ectoine production, the changes in the pH concomitant to the production of organic acids and alcohols, and the anaerobic restrictive conditions characteristic of acetogens. The use of mixotrophs also appears as a solution for ectoine production from CO_2/CO. In fact, recently, it was observed that *H. elongata* anaplerotic flux can support an increase in ectoine production when using glucose as the main carbon source (Hobmeier et al. 2020). In other study, the addition of low concentrations of glucose (0.5 g L^{-1}) to *Halomonas stevensii* cultures promoted ectoine contents of 15% and 22% at salinities of 6% and 12% NaCl, and supported an abatement of 37.1 mg CO_2 L^{-1} h^{-1} (Cantera et al. 2022). Besides glucose, other organic compounds, such as

acetate and alcohols, could be considered for mixotrophic growth, though they have not yet been experimentally tested.

Nevertheless, a chemoautotrophic biotechnological platform that allows to produce ectoines purely with CO_2 as the sole carbon source has a great potential. Although, dark fixation provides less energy than aerobic respiration of sugars, this bioconversion process could use CO_2 from industrial flue gases, and waste gases (CO, H_2) or liquid waste (sulfur compounds, metals, ammonium) as energy source enhancing the feasibility and expansion of this residue-valorisation technology. Moreover, it could be implemented in both, aerobic and anaerobic conditions. However, CO_2 and CO have been disregarded for the production of ectoines, fact that is probably related to the current lack of fundamental studies proving that chemolithoautotrophs can produce ectoines.

Potential chemolithoautotrophs able to produce ectoines

Although heat or cold stress can affect ectoine accumulation, salinity is the main trigger for the expression of genes involved in ectoine biosynthesis pathway (Argandoña et al. 2021). Thus, ectoine and hydroxyectoine production is usually observed in halophilic or halotolerant organisms. Several halophiles have the ability to grow on CO_2 and/or CO, but their potential to produce ectoines while using these gases is unexplored. Based on literature and genomic databases (supplementary information 2), we gathered a total of 143 species of halophilic chemolithotrophs, carboxydotrophs and carboxydovores. All the identified species that were able to use CO_2 and CO aerobically and anaerobically, together with their required energy sources and their optimum salinity for growth are summarized in supplementary information 2, Table S4 and Table S5. Genomes of the identified species were screened for genes encoding for enzymes involved in the ectoine and hydroxyectoine synthesis pathways: specifically *ectA*, *ectB*, *ectC* and *ectD* (supplementary information 2, Tables S6 and S7). Moreover, the presence of *ectR*, an important transcriptional regulator of this pathway, and two genes involved in the production of the precursor L-2,4-diaminobutyrate (aspartate kinase: *ask* and aspartate semi-aldehyde dehydrogenase: *asd*), were assessed.

In total, 31 microbial genomes were identified with the *ectABC* gene cluster (Figure 2). Most of these genomes (22) belonged to aerobic organisms capable of CO_2 fixation. Some of them are well described as pure chemolithotrophs that use H_2 (*Alkalilimnicola ehrlichii, Hydrogenovibrio marinus, Pseudonocardia autotrophica, Pseudonocardia dioxanivorans, Rhodococcus opacus*), $S_2O_3^-$ (*Guyparkeria halophila, Halothiobacillus neapolitanus, Salinisphaera hydrothermalis, Thiohalomonas denitrificans, Thiomicrospira aerophila, Thiomicrospira halophila*), NH_4^+ (*Nitrosococcus halophilus, Pseudonocardia ammonioxydans*), NO_2^- (*Nitrococcus mobilis*) or Fe^{2+} and reduced sulfur compounds (*Acidihalobacter aeolianus, Acidihalobacter ferrooxidans, Acidihalobacter prosperus*) as electron donors. This diversity indicates a broad range of possibilities for application in biotechnological processes. Some anaerobic chemolithoautotrophs also contained the genes for ectoine synthesis. These included *Achromobacter ruhlandii*

and *Alkalilimnicola erlichii* (CO_2 fixation with H_2 as electron donor and NO_3^- as electron acceptor), *Desulfatibabacillum aliphaticivorans* (CO_2 fixation with H_2 as electron donor and SO_4^{2-}as electron acceptor), *Desulfocapsa sulfexigens* (CO_2 fixation with H_2 as electron donor and S^0, SO_3^{2-}, $S_2O_3^{2-}$ as electron acceptors), and the methanogen *Methanobacterium subterraneum* (CO_2 fixation with H_2 as electron donor). Theoretically, these could be potential candidates for the anaerobic conversion of CO_2 into ectoine.

As less CO-utilizing microbes are known, and therefore screened, their metabolic potential may be less well characterised. However, some aerobic carboxydotrophs such as *Hydrogenibacillus schlegelii, and Hahella chejuensis,* aerobic carboxydovores, such as *Alkalispirillum mobile* and *Mycobacterium smegmatis*, and the facultative anaerobe *Alkalilimnicola erlichii* were detected as putatively able to consume CO and produce ectoine (Hoeft et al. 2007).

The formation of hydroxyectoine depends on the initial synthesis of ectoine and its subsequent hydroxylation by the enzyme coded by the gene *ectD*. The *ectD* gene was found in 14 of the genomes that contained *ectABC*. Ten of those genomes belonged to aerobic CO_2-utilizing microbes (Figure 2), one to an anaerobic chemolithoautotrophic CO_2 consumer (*Achromobacter ruhlandii*), and three to aerobic CO-utilizing microbes (*Mycobacterium smegmatis*, *Hydrogenibacillus schlegelii,* and *Hahella chejuensis*).

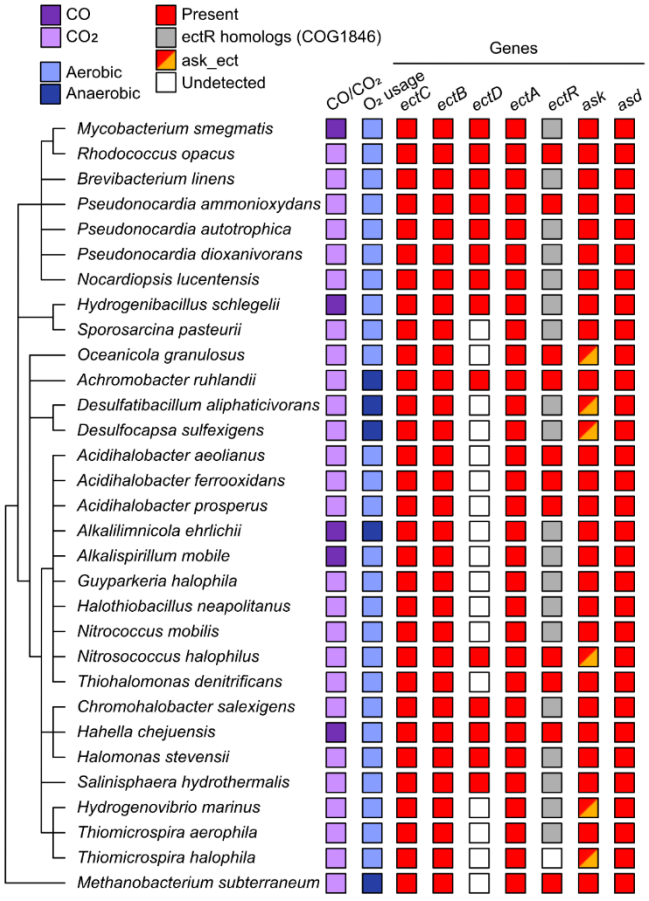

Figure 2. Presence/absence of ectoine biosynthesis genes in halophilic chemolithotrophs. All genomes found with *ectC* and *ectB* were interrogated for other relevant genes in the ectoine biosynthesis pathway. All detected *ectA* and *ectD* were found within 10 kb of *ectB* and *ectC*. All surveyed genomes contained aspartate kinase (*ask*) genes. Additionally, *ask* copies found within 10 kb of the *ect* gene cluster are considered to represent *ask_ect* orthologs (orange). While most genomes contained genes belonging to the *ectR* gene family (COG1846; gray), only those found within 10 kb of the ect gene cluster were considered *ectR* orthologs (red). The phylogeny displayed at the left reflects the relationships between organisms based on their NCBI taxonomy.

Perspectives

This work sheds light in a new direction looking at yet overlooked microbes and strategies that can help in the development of CO_2 and CO valorization. The information provided has the potential to propel new research in this topic for different industrial scenarios, using H_2, nitrogen and sulfur compounds or metals as the energy source. Moreover, the approaches and results from this review are applicable for the valorization of any CO_2-containing gases, including emissions from industrial sites (steel mills, cement producers, electricity plants, etc.); flue gas emissions (natural gas-fired power plants, coal boilers) and syngas. Besides, biotransformations carried out at high salinity can be adapted to reduce cost (use of plastic-based reactors, sea water as medium) and are usually more robust processes due to the low risk of contamination. Therefore, this review offers a completely new strategy that can pave the way for a more cost-effective elimination of GHG and waste gasses, as well as more sustainable and circular chemical production systems.

Declarations

The authors have no relevant financial or non-financial interests to disclose.

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