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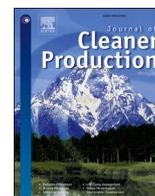
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Environmental life cycle assessment of production of the non-nutritive sweeteners aspartame (E951) and neotame (E961) from chemical processes: The SWEET project

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ABSTRACT

Consumption of added sugar is a cause of concern due to links with non-communicable diseases. Non-nutritive sweeteners (NNSs) are increasingly seen as a viable alternative. Health and safety of NNSs are well studied, but not their environmental impact. In this study the environmental impact of NNSs aspartame and neotame are presented. This is the first such study attempting to quantify environmental impact of neotame. Life cycle data are derived from literature, alongside stoichiometric reaction equations and resulting heat changes. Global warming potential (GWP) of 1 kg aspartame is found to be 29.25 kgCO₂-eq/kg, and 1 kg neotame to be 43.42 kgCO₂-eq/kg. It is found that both NNSs have great potential to replace the sweetness of added sugar with reduced environmental impact, e.g., GWP of neotame is found to be 0.4–0.7%, and aspartame 10.5–18.4%, of an equivalent sweetness for sucrose. This study demonstrates that environmental impact of the additional resources required to make neotame from aspartame are more than offset by the increase in perceived sweetness, from 200 to 8000-times. It is shown that there are significant uncertainties related to life cycle inventory data and data derivation method. Therefore, this work further highlights the difficulties of conducting a life cycle assessment of highly refined industrial food additives and the need for good industrial collaboration in obtaining data.

1. Introduction

Added sugar within consumers' diets is increasingly being scrutinized for its possible links with non-communicable diseases such as tooth decay (Vaghela et al., 2020), and obesity (Johnson et al., 2017). There is potential for non-nutritive sweeteners (NNSs) to mitigate these health issues by replacing the sweetness of added sugar in food and beverage products (O'Connor et al., 2021; McGlynn et al., 2022) and the World Health Organization recently published an extensive review of

literature relating to health effects of consuming NNSs (Rios-Leyvraz and Montez, 2022). Regardless of the health implications, any authorized NNS must have first undergone a rigorous safety approval process as outlined in Regulation EC 1333/2008 (EC, 2008).

Two such authorized NNSs are aspartame and neotame. Aspartame was first patented in 1970 (Schlatter, 1970), is identified as additive E951, and is one of the most widely used and consumed NNSs (Le Donne et al., 2017; Buffini et al., 2018; Hafner et al., 2021). It is authorized for consumption in the EU and, due to its prevalence, it was one of the first

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additives to undergo the EFSA safety re-evaluation (EFSA, 2013). Aspartame is a secondary amine that is industrially produced either from bio-production or chemical processes (Yagasaki and Hashimoto, 2008). It has a high sweetness that is approximately 200-times that of sugar (EFSA, 2013). Neotame was first patented in 1996 (Claude and Tinti, 1996), authorized for use in the EU in 2007 (EFSA, 2007), and is identified as additive E961. Neotame is derived from aspartame through addition of a 3,3-dimethyl butyraldehyde functional group, which increases apparent sweetness to approx. 8000-times that of sugar (Palazzo et al., 2011; Wal et al., 2019).

In parallel with food safety, there is significant concern relating to environmental impact of foods (e.g., Behrens et al., 2017; Ibarrola-Rivas and Nonhebel, 2022). However, existing food-based or dietary studies do not explicitly include the impact of NNSs. Indeed, the authors are aware of only six LCA for NNSs, limited to the ingredient level; five studies for steviol glycosides (PureCircle, 2015; Cargill, 2021; Gantelas et al., 2022; Milovanoff and Kicak, 2022; Suckling et al., 2023b), one for aspartame in the World Food LCA Database (WFLDB, Nemecek et al., 2019); and one further study for the sweetness enhancer, thaumatin (Suckling et al., 2023a). For the WFLDB aspartame LCA, the precursor amino acids are produced by bacterial fermentation and combined to make aspartame via chemical synthesis. Environmental impact data of aspartame from the WFLDB LCA are reported in Section 4 by way of comparison to those from this study and to understand differences. Another production route, one based primarily on chemical synthesis, is also widely used (Yagasaki and Hashimoto, 2008) and at present an LCA study of this is lacking, a gap which needs to be filled.

Understanding the sustainability of the foods and their ingredients is increasingly important, especially if there is a desire to replace added sugar with alternatives such as NNSs for health reasons alone. However, in order to understand potential ramifications for sustainability of making the swap at a dietary level, it is first necessary to have sufficient LCAs at an ingredient level. At present, the existing studies are predominantly related to stevia variants, with other NNSs underrepresented. Further research into other NNSs is important to enable a more balanced dietary study. Therefore, this study aims to fill the gap by making available further data for the NNSs aspartame and neotame.

The primary objectives were an environmental life cycle assessment (LCA) for both aspartame and neotame produced primarily via chemical processes, and to understand whether production of both sweeteners caused less impact than the equivalent sweetness of sugar. However, an LCA is data intensive, and accurate primary data are essential in allowing precise understanding of environmental impact. The NNS industry is small, and there are heightened concerns relating to intellectual property (from private communications with manufacturers), making it difficult for manufacturers to divulge commercially sensitive information. Therefore, to begin to understand environmental impact of NNSs, or other refined chemical compounds, it might be necessary to proceed without primary data. Different methods have been developed, such as use of material proxies (Mila i Canals et al., 2011), resource requirements derivations from stoichiometric reaction equations (Hischier et al., 2005) or molecular structure (Wernet et al., 2008), and the RREM method for building chemical life cycle inventory (Huber et al., 2022). This study took a similar approach by deriving life cycle data from literature, with further data derived from stoichiometric reaction equations and energy balances for each synthesis step. Therefore, the results presented here provide a first estimate of environmental impact for neotame, and aspartame derived from chemical processes, and explore issues associated with attempting such as study on industrially derived refined food additives. Inevitably, the data and derived results are subject to a degree of uncertainty, which is explored in this study, and it is hoped that further collaboration with industry would address and mitigate potential issues of bias in data estimation. To facilitate openness of the research, and enable other practitioners to interrogate the results, and test assumptions made, the data file export from SimaPro is provided as Supplementary Material ("LCI Export.

CSV").

The research questions of this study are:

- 1) What is the environmental impact of producing 1 kg aspartame, and subsequently 1 kg neotame?
- 2) What is the sensitivity of the baseline impact results to process data uncertainty?
- 3) What is the net environmental impact of the two NNSs in terms of replacing an equivalent sweetness of added sugar?

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2. Overview of production process and LCA

Fig. 1 shows the main LCA modelling processes used to calculate environmental impact of 1 kg aspartame, and separately, 1 kg neotame. The system boundary is marked with a dashed box and flows of resources and emissions accounted for indicated. All emissions relating to background processes are also accounted for. For aspartame production, the two main inputs are L-phenylalanine methyl ester hydrogen chloride (L-PheMEHCl), and N-carbobenzoxy-L-aspartic acid (Z-Asp acid). Results of this study are reported in terms of impacts of producing each of the four materials. However, neither L-PheMEHCl nor Z-Asp acid were found in the Ecoinvent database. Therefore, it was necessary to develop production pathways back to materials which were available. The process of achieving this is described in subsequent sections.

Impact assessment was conducted using SimaPro 9.3 software and Ecoinvent 3.3 database (Wernet et al., 2016), and the ReCiPe 2016 Midpoint (Hierarchist) method (Huijbregts et al., 2016). Environmental impact within all ReCiPe 2016 impact categories is reported, with focus on global warming potential, land use, water consumption and mineral resource scarcity.

2.1. Functional unit, goal, and scope

The goal of the LCA was to assess environmental impact of producing aspartame (E951), and subsequently neotame (E961), from a chemical production process. The LCA was cradle-to-factory-gate, and functional units are, separately, "production of 1 kg purified aspartame" and "production of 1 kg purified neotame". Both NNSs can be used in a variety of applications and, therefore, their use in food or beverage products was omitted as out of scope. The factory was not modelled as being in a particular location and, therefore, global mixes of materials and energy were used where possible.

The study included all steps in synthesis of materials, from those present in the Ecoinvent database, up to purified aspartame and neotame. All foreground data for materials consumption and emissions were derived from literature, and further data relating to energy consumption were calculated through study of stoichiometric reaction equations and known chemical properties. The approach is outlined in more detail in Sections 2.3 and 3. Background activities were included for inputs such as energy, materials, and infrastructure. All wastes and otherwise unrecovered materials were assumed emitted, unchanged, into the environment.

The LCA was conducted in line with the ISO 14040:2006 (ISO, 2010a) and ISO 14044:2006 (ISO, 2010) standards.

The functional unit was mass because it is an SI unit. However, mass does not represent the functional use of any NNSs, which are perceived as being much sweeter than sugar (specifically, sucrose). Therefore, they are described in terms of 1 kg "sweetness equivalence", or "sucrose equivalence" (SE and subsequently 1 kg_{SE}). Aspartame has an SE of approximately 200-times that of sugar (EFSA, 2013), and neotame approximately 8000-times (Wal et al., 2019). Therefore, results will also be presented in discussion in terms of 1 kg_{SE} for both aspartame and

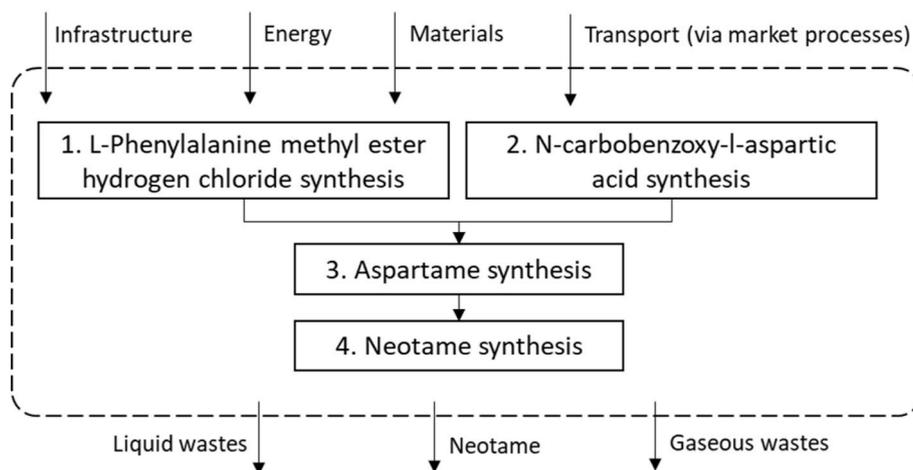


Fig. 1. Life cycle assessment process modelling steps and system boundaries (dashed box). Results reported in terms of main aspartame reagents and product NNSs (black boxes).

neotame, i.e., in terms of 5 g aspartame, and 0.125 g neotame.

2.2. Allocation of impacts

All impacts were associated with either aspartame or neotame. When aspartame is the final product, all impacts are allocated to it. When neotame is the final product, it is assumed that all the aspartame is consumed for neotame production and, therefore, all impacts are allocated to neotame.

Cut-off criteria were applied to by-products entering or leaving the system. In this regime, no burden is allocated to by-products from NNS

synthesis but, likewise, they carry no benefits if recycled. Impacts from wastes emitted to the environment and treatment of wastes are accounted for.

2.3. Assumptions

On order to calculate the life cycle inventory, several assumptions were used to enable conversion of information presented in background literature to quantities of materials and energy consumed in the production process.

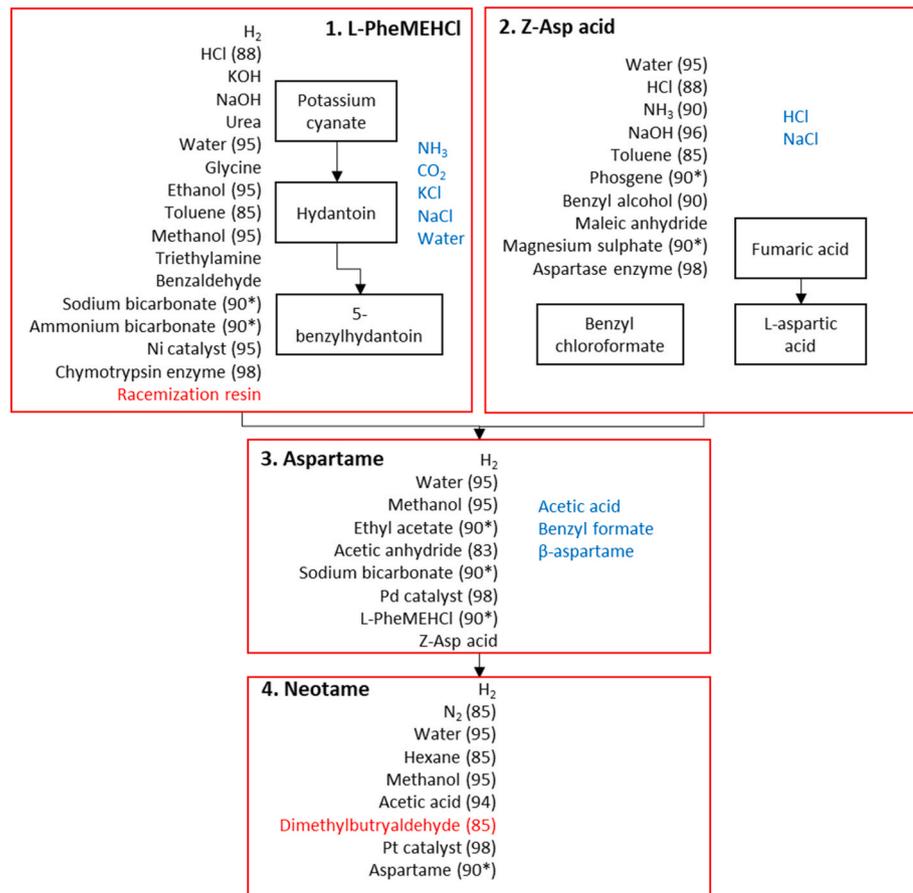


Fig. 2. Production process of aspartame and neotame showing inputs and outputs from main synthesis steps (red boxes) for 1) L-PheMEHCl, 2) Z-Asp acid, 3) Aspartame, and 4) Neotame. Also shown are synthesis sub-steps (black boxes). Materials consumed are listed as black text, and emission as blue. Recovery rates (in %) are in brackets, and assumed rates denoted by ‘*’. Materials in red text are proxies which are tested in scenario modelling. Abbreviations listed in Supplementary Material, Section 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

2.3.1. Assumption: synthesis and material recovery

It was not possible to determine where the synthesis steps associated with Z-Asp acid, L-PheMEHCl, aspartame, and neotame took place. Therefore, it was assumed that each is produced in their own factories, with all input materials sourced from commodities markets. For each of steps 1–4, in Fig. 1, material recovery rates were defined and used as a parameter in the life cycle impact assessment modelling. Material recovery rates were sourced from literature where possible, and are given in Supplementary Material, Table S9, and shown in Fig. 2 in brackets next to material names. Where references could not be found, a 90% recovery rate was assumed (denoted with an ‘*’, Fig. 2), based upon the average of the referenceable recovery rates in Table S9 (approx. 91.8%). This base assumption for recovery rates differs from the RREM method by Huber et al. (2022) due to the more focused nature of this study into two products, as opposed to a broad portfolio of 60 chemicals. However, recovery rates found in literature might be specific to the system from which the material is recovered, and not directly applicable to the process used here. Therefore, sensitivity analysis explored a $\pm 10\%$ change in recovery rate, or if recovery rate was already $\geq 90\%$, then 100% was assumed. Extra resources for recovery of materials within the production process could not be identified in literature and are therefore omitted from this study. Reaction products that were not otherwise re-used within the synthesis process were assumed to be emitted into the medium in which they were created, e.g., carbon dioxide (CO₂) to air, or sodium chloride (NaCl) to water. Likewise, input materials (such as reagents, solvents or catalysts) which were not recovered, were assumed emitted, unchanged, into the environment. This differs from the approach used by Huber et al. (2022), in which such materials were treated as hazardous waste, and from the aspartame model in the WFLDB, in which such materials are treated by wastewater treatment plant. Therefore, different treatment methods are explored in scenario modelling, Section 5.1. All recovery rates are parameterized in the Supplementary Material, “LCI Export.CSV”, and can be further tested by practitioners.

2.3.2. Assumption: reactions

Literature may state reagents and yields in a chemical synthesis but does not always state by-products or side-products of a reaction. Therefore, where yields are not stated, it is assumed that reagents are recovered (subject to a recovery rate), kept within the system, and recirculated for as long as they can be used. A similar approach is used by Huber et al. (2022) in the RREM method. Where other reaction products were not specified, but are expected due to the reaction taking place, stoichiometric equations were used to identify possible products and quantities produced. For this study, any materials not recovered are assumed emitted to the environment, an assumption which differs from Huber et al. (2022). Alternative disposal methods for such emitted materials are explored in scenario modelling (Section 5.1). For aspartame, yield of both alpha- and beta-aspartame are given, and these are used in mass calculations.

2.3.3. Assumption: energy consumption

Literature will state reaction conditions in terms of heating, cooling, or temperature, but rarely the energy required to achieve those conditions. Sometimes, it is possible to use chemical process software (e.g., Aspen Plus) to calculate energy requirements, but only if the materials are present in the databases. At the time this study was conducted, many required materials could not be found in the Aspen Plus database. An alternative is to use a baseline quantity for calculations, as tested by Huber et al. (2022), which used 0.5 kWh/kg product. For this study energy consumption was estimated based upon stoichiometric equations, molecular structure, and phase changes, and reported masses used within reactions. Therefore, Microsoft’s Excel was used to estimate energy consumption as follows:

- 1) *Enthalpy*: an estimate of heat energy emitted or consumed by a reaction was made based upon the molecular structure and mass of both reagents and products of each synthesis step.
- 2) *Heat*: energy required to change the temperature of a material, or mixture, was estimated based upon the average specific heat of all materials in a mixture. Energy required for both heating and cooling were included.
- 3) *Vaporization*: heat energy consumed in evaporating liquids under reflux were included based upon the specific heat of vaporization of all materials. It was assumed that the entire mass of materials was evaporated once during reflux.
- 4) *Stirring*: electrical energy consumed in mixing or stirring reaction was estimated based upon the total mass of materials in a given synthesis step and indicative motor power rating.
- 5) *Pumping*: electrical energy consumed in pumping gases was included for instances when a gas was passed through a liquid (for example, nitrogen purging or hydrogenation). The mass of gas pumped, and indicative pump power ratings were used.

For changes due to enthalpy, temperature, and vaporization, fundamental material properties were sought from either the NIST Chemistry WebBook (NIST, 2022) or, if information was not available there, NCBI PubChem (NCBI, 2022). Where data were not found, these were approximated by combining values of precursor materials (if a reaction joined the two), or by averaging values of products (if a reaction split a molecule). When mixtures of materials were heated or cooled, an average specific heat capacity for a mixture was derived from the individual component material properties. Information relating to derivation of energies, including stoichiometric equations, is given in Supplementary Material, Sections 2, 3, 4.2, and Tables S2, S4, S6, S8, and S10-S13.

It was assumed that 85% of heat energy could be recovered. This assumption was subject to a $\pm 10\%$ variability for scenario modelling (Section 5.1). In contrast, it was assumed that electrical energy used for stirring and pumping could not be recovered. However, it is acknowledged that both stirring and pumping may result in heat change of the materials being manipulated, but this was omitted from calculations. Finally, the entire process was assumed to occur under isobaric conditions, such that temperature changes due to expansion or contraction of volumes were omitted.

This approach differs from the RREM method developed by Huber et al. (2022) for which a baseline thermal energy consumption of 0.5 kWh/kg product was used. Therefore, energy consumption is tested in scenario modelling (Section 5.1) to understand sensitivity of the results presented in this study to such change. Furthermore, energy consumption is a parameter which may be changed in the Supplementary Material process model file for further analysis by LCA practitioners.

3. Life cycle inventory

In this section, life cycle inventory (LCI) data are given in terms of a 1 kg reference mass for each of the main materials: L-PheMEHCl, Z-Asp acid, aspartame, and neotame. Fig. 2 shows the main synthesis steps (red boxes) and further synthesis sub-steps to go from a material to the Ecoinvent database (black boxes). Also shown are the materials consumed (left hand side, black text) and emitted (right hand side, blue text). Numerals in brackets after the materials are recovery rate percentages, with those subject to assumption denoted by a ‘*’. Further details of recovery rates are given in Supplementary Material, Table S9. Materials without a recovery rate are completely consumed or emitted without recovery. Materials which were subject to scenario modelling are shown in red text. Data relating to materials and energy consumption modelled for baseline environmental impact are described in Section 3.1 - 3.4 and given in Tables 1–4. A full description of the individual synthesis steps is given in Supplementary Material, Section 5, and raw data, which assumes no recovery rate, are given Supplementary

Table 1
Life cycle inventory data for production of 1 kg L-PheMEHCl.

L-PheMEHCl synthesis			
Inputs	Inputs per 1 kg	Outputs per 1 kg	Notes
Potassium hydroxide	298.26 g		
Urea	638.52 g		
Glycine	399.08 g		
Hydrogen chloride	931.28 g	60.88 g	
Water	330.99 g	687.79 g	Includes by-product water.
Benzaldehyde	553.91 g		
Ammonium bicarbonate	10.41 g	10.41 g	
Ethanol	23.99 g	23.99 g	
Nickel	1.91×10^{-1} g	1.91×10^{-1} g	
Triethylamine	2.60×10^{-2} g		
Hydrogen	9.28 g		
Sodium hydroxide (NaOH)	185.60 g		
Methanol	631.52 g	334.39 g	
Toluene	600.45 g	600.45 g	
Sodium bicarbonate	818.42 g	38.97 g	
Enzyme (alpha amylase)	1.33×10^{-2} g	1.33×10^{-2} g	Proxy for chymotrypsin. Emission modelled as an unspecified organic substance.
Factory	3.38×10^{-11} units		
Heating	1.18×10^{-4} kWh		
Electricity	8.36×10^{-3} kWh		
Ammonia		350.63 g	
Carbon dioxide		642.34 g	
Potassium compounds		396.34 g	Proxy for potassium chloride emission.
NaCl		542.34 g	

Table 2
Life cycle inventory data for production of 1 kg Z-Asp acid.

Z-Asp acid synthesis			
Inputs	Inputs per 1 kg	Outputs per 1 kg	Notes
Maleic anhydride	942.22 g		
Benzyl alcohol	650.01 g	15.38 g	
Phosgene	613.90 g	32.80 g	
Enzyme (alpha amylase)	5.87 g	5.87 g	Proxy for aspartase on beads. Emission modelled as unspecified organic substances.
Magnesium sulphate	1.50×10^{-1} g	1.50×10^{-1} g	
Toluene	155.89 g	155.89 g	
Water	782.66 g	686.84 g	
Sodium hydroxide (NaOH)	178.47 g	7.05 g	
Ammonia	78.52 g	5.56 g	
Hydrogen chloride	23.24 g	237.05 g	
Factory	3.38×10^{-11} units		
Heating	4.81×10^{-5} kWh		
Cooling	1.13×10^{-1} kWh		
Electricity	2.27×10^{-2} kWh		
NaCl		218.74 g	

Table 3
Life cycle inventory data for production of 1 kg Aspartame.

Aspartame synthesis			
Inputs	Inputs per 1 kg	Outputs per 1 kg	Notes
Z-Asp acid	1118.75 g		
L-PheMEHCl	940.80 g		
Acetic anhydride	467.40 g	14.56 g	
Ethyl acetate	1033.20 g	1033.20 g	
Sodium bicarbonate	386.58 g	15.38 g	
Palladium	1.49×10^{-2} g		Proxy for Pd on activated carbon.
Hydrogen	8.39 g		
Methanol	249.20 g		
Water	5656.2 g	5735.88 g	Includes by-product water.
Factory	3.38×10^{-11} units		
Heating	11.06 kWh		
Electricity	4.31×10^{-2} kWh		
Carbon dioxide		194.70 g	
Acetic acid		503.87 g	
Organic substance		32.58 g	Proxy for L-PheME.
Benzyl acetate		569.99 g	Proxy used for benzyl methanoate.
Sodium chloride		258.60 g	
Aspartame		234.60 g	Proxy for beta-aspartame.

Table 4
Life cycle inventory data for production of 1 kg Neotame.

Neotame synthesis			
Inputs	Inputs per 1 kg	Outputs per 1 kg	Notes
Aspartame	813.64 g	35.86 g	
Cyclohexanol	311.82 g	47.25 g	Proxy for 3,3-dimethylbutyraldehyde
Platinum catalyst	2.27×10^{-1} g	2.27×10^{-1} g	Proxy for Pt on activated carbon.
Acetic acid	81.82 g	81.82 g	
Water	613.64 g	613.64 g	
Nitrogen	3409.09 g	3409.09 g	
Hexane	1123.41 g	1123.41 g	
Hydrogen	7.72 g		
Methanol	270.00 g	270.00 g	
Factory	3.38×10^{-11} units		
Heating	1.27 kWh		
Electricity	1.48×10^{-3} kWh		

Material, Tables S1–S8. Conversion from raw data to that presented in the LCI is via equations given in Supplementary Material, Section 4.1. Stoichiometric equations used in calculations are given in Supplementary Material, Section 2, and materials properties used for energy calculations are given in Supplementary Material, Tables S10–S13.

3.1. L-PheMEHCl synthesis

L-PheMEHCl production (box 1, Fig. 2) is comprised of several synthesis steps to get back to the Ecoinvent database. These are summarized in this section, and aggregated LCI data given in Table 1.

3.1.1. L-PheMEHCl

L-PheMEHCl synthesis data were derived from Mirviss et al. (1990). 5-benzalhydantoin is hydrogenated to 5-benzylhydantoin in the presence of a Raney nickel catalyst in triethylamine. The 5-benzylhydantoin is refluxed with NaOH in water to produce D,L-phenylalanine (D,L-Phe) and by-product ammonia and CO₂. The solution is neutralized with HCl,

creating by-product NaCl. Then, D,L-phenylalanine is refluxed in methanol and HCl, and neutralized with sodium bicarbonate, to produce D,L-phenylalanine methyl ester (D,L-PheME), and by-product NaCl, CO₂ and water.

Only L-PheME can be used for aspartame synthesis. Therefore, D-PheME and L-PheME are separated by hydrolyzing L-PheME with immobilized chymotrypsin enzyme in the presence of water and toluene. Alpha-amylase is used as a proxy for chymotrypsin. The D-PheME is racemized in the presence of a resin. Racemization produces at best a 50:50 mix of the D- and L-PheME isomers. Therefore, it is assumed that process racemization has reached a steady state, and that resources required for 100% racemization are double those derived from Mirviss et al. (1990).

Multiple resins were explored by Mirviss et al. (1990), including some derived from “strong base anionic exchange resins”. However, production routes for the resins could not be further identified, and no direct equivalents were found in available LCI databases. Moreover, the quantity of resin used was not well defined, and was stated as being “recycled 4 times without any loss in activity”. Therefore, for baseline impact calculations, it was assumed the resin is re-used indefinitely, and omitted from the LCA. However, resin consumption is explored in scenario modelling (Section 5.1).

3.1.2. 5-Benzylhydantoin

5-Benzylhydantoin synthesis data were derived from Mirviss (1986). Hydantoin and benzaldehyde are refluxed in the presence of water and ammonium bicarbonate. Additional water is produced from the reaction. The product is washed with further water and ethanol.

3.1.3. Hydantoin

Hydantoin synthesis data were derived from Royal Society Chemistry website and stoichiometric equations because no other reference could be found (RSC, 2022). Glycine, potassium cyanate and HCl are reacted to produce hydantoin, and by-product water, and potassium chloride.

3.1.4. Potassium cyanate

Potassium cyanate synthesis data were derived from pattern US 3,395,300 (Tucker and Blanton, 1976). Potassium hydroxide and urea are mixed together and heated until weight loss has stopped. It is assumed that weight loss is due to emission of CO₂ and NH₃ from the reaction.

3.2. Z-aspartic acid synthesis

Z-Asp acid production (box 2, Fig. 2) is comprised of several synthesis steps to get back to the Ecoinvent database. These are summarized in this section, and the aggregated LCI data given in Table 2.

3.2.1. Z-aspartic acid

Z-Asp acid synthesis data were derived from US 4,435,091 (Sugiyama et al., 1982). L-aspartic acid, benzyl chloroformate and NaOH are reacted to produce Z-Asp acid, and by-product water and NaCl. The reaction takes place in the presence of water, toluene and pH is adjusted using 35% HCl.

3.2.2. L-aspartic acid

L-aspartic acid synthesis data were derived from EP 0952225 A2 (Mukouyama and Komatsuzaki, 1999). Fumaric acid is reacted with ammonia, to produce L-aspartic acid, in the presence of NaOH, water, magnesium sulphate, by passing through a column of aspartase enzyme coated beads. Alpha-amylase is used as a proxy for aspartase.

3.2.3. Fumaric acid

Fumaric acid is modelled using maleic acid as a proxy because the two are trans-isomers and the precursor, maleic anhydride, is available

in the Ecoinvent database. Maleic anhydride is hydrolyzed to form maleic acid. Stoichiometric quantities are used in modelling.

3.2.4. Benzyl chloroformate

Benzyl chloroformate synthesis data were derived from US 6,696,590 (Bonnard et al., 2004). Benzyl alcohol is reacted with phosgene under reflux to form benzyl chloroformate and by-product HCl.

3.3. Aspartame

Aspartame synthesis (box 3, Fig. 2) data were derived from US 3,786,039, example 5 (Ariyoshi et al., 1974), which discloses a chemical (as opposed to biological) process. LCI data are given in Table 3. First, Z-Asp acid is reacted with acetic anhydride, in the presence of ethyl acetate, to produce Z-Asp anhydride and by-product acetic acid. In parallel, L-PheMEHCl is reacted with sodium bicarbonate, in the presence of water and ethyl acetate to form L-PheME and by-product NaCl, CO₂ and water.

Next Z-Asp anhydride is reacted with the L-PheME in the presence of ethyl acetate. N-carbobenzoxy-L-aspartyl-L-phenylalanine methyl ester crystals form which are dissolved in methanol and water before being hydrogenated in the presence of sodium bicarbonate and palladium catalyst on activated carbon to produce aspartame, and by-product benzyl formate. The resulting crystals are dissolved in water to separate the alpha-L-Asp-PheME (aspartame and 81% yield) and non-sweet tasting beta-L-Asp-PheME (19 %yield). The beta isomer is discarded but modelled using aspartame as a proxy for emissions purposes.

3.4. Neotame

Neotame synthesis (box 4, Fig. 2) data were derived from US 5,511,508 (Claude and Tinti, 1996). LCI data are given in Table 4. Aspartame is reacted with 3,3-dimethyl butyraldehyde in the presence of acetic acid in water, methanol and 5% platinum catalyst on activated carbon. The product is hydrogenated to produce neotame and by-product water. Nitrogen purging is used before and after hydrogenation. Lastly, the solution has its pH raised to 5 by NaOH. The solid product is washed with hexane.

No production pathway for 3,3-dimethyl butyraldehyde could be found to the Ecoinvent database. Therefore, cyclohexanol was used as a proxy because its formula is also C₆H₁₂O. However, environmental impact can be due to other factors, such as functional group, and sensitivity to change in proxy is explored in Section 5.1.

3.5. Regarding total energy consumption

Energy consumption is presented in terms of electricity (for pumping and stirring), and heating, vaporization, and cooling for each synthesis step. For L-PheMEHCl and Z-Asp acid the synthesis step heat requirements (1.18×10^{-4} kWh/kg and 1.13×10^{-1} kWh/kg respectively) are lower than those predicted by Huber et al. (2022). However, for the final products, total heat consumption is 11.07 kWh/kg for aspartame and 10.38 kWh/kg for neotame. These are in excess of an estimated 4.62 kWh/kg for aspartame and 4.26 kWh/kg for neotame (after accounting for masses of materials passing between synthesis steps, and assuming 0.5 kWh/kg per precursor material production step). Another point of reference is the aspartame model in the WFLDB (Nemecek et al., 2019), which reports 1.36×10^{-1} kWh/kg electrical energy and 2.59 kWh/kg heat energy. In this study, net foreground electrical energy consumption was assumed to be 7.64×10^{-2} kWh/kg for aspartame, and 6.36×10^{-2} kWh/kg for neotame. Therefore, baseline consumption of electrical energy in this study is lower, and heat energy is higher, than that of the WFLDB. Change in energy consumption is explored in scenario modelling for both electrical and heat energy (Section 5.1).

4. Results

In this section, results are presented in terms of producing 1 kg aspartame, and 1 kg neotame separately.

Fig. 3 shows relative contribution to environmental impact of 1 kg aspartame from Z-Asp acid (red), L-PheMEHCl (grey), and the aspartame synthesis step (black). Numerical data are given in Table 5. In terms of GWP, net impact of 1 kg aspartame production is 29.25 kgCO₂-eq/kg. Within this, the aspartame synthesis step accounts for 9.91 kgCO₂-eq/kg, Z-Asp acid 8.37 kgCO₂-eq/kg, and L-PheMEHCl 10.96 kgCO₂-eq/kg. In terms of LU, net impact is 5.87 × 10⁻¹ m²acrop-eq/kg, with contribution from the aspartame synthesis step of 1.73 × 10⁻¹ m²acrop-eq/kg, Z-Asp acid 1.89 × 10⁻¹ m²acrop-eq/kg, and L-PheMEHCl 2.25 × 10⁻¹ m²acrop-eq/kg. In terms of MRS, net impact is 9.98 × 10⁻² kgCu-eq/kg, with contributions from aspartame synthesis of 4.75 × 10⁻² kgCu-eq/kg, Z-Asp acid 1.90 × 10⁻² kgCu-eq/kg, and L-PheMEHCl 3.33 × 10⁻² kgCu-eq/kg. Finally, in terms of WC, net impact of aspartame production is 4.90 × 10⁻¹ m³/kg, with contribution of aspartame synthesis of 1.46 × 10⁻¹ m³/kg, Z-Asp acid 1.28 × 10⁻¹ m³/kg, and L-PheMEHCl of 2.16 × 10⁻¹ m³/kg. The impact is reasonably evenly distributed across each of the three groupings shown in Fig. 3. Across all impact categories, aspartame synthesis accounts for an average of 33.1% net impact, Z-Asp acid 23.1%, and L-PheMEHCl 43.8%.

For comparison, environmental impact of aspartame from the World Food LCA Database (WFLDB) (Nemecek et al., 2019) is 89.60 kgCO₂-eq/kg for GWP, 18.51 m²acrop-eq/kg for LU, 4.90 × 10⁻¹ kgCu-eq/kg or MRS, and 4.25 m³/kg for WC. This is significantly greater than results shown here. However, there are key differences that account for much of the difference. Firstly, in WFLDB, L-phenylalanine is the precursor material, and not L-PheMEHCl, as used here. Secondly, both L-phenylalanine and Z-Asp acid are derived from fermentation, and their contributions to net impact are on average 49.1% and 39.6%, respectively, across all impact categories, greater than either contribution in this study. Accounting for those differences, the aspartame synthesis steps are otherwise similar (presented in order of this study to WFLDB): for GWP, 9.91 to 6.85 kgCO₂-eq/kg; for MRS, 4.75 × 10⁻² to 5.74 × 10⁻² kgCu-eq/kg; and for WC 4.90 × 10⁻¹ to 4.70 × 10⁻¹ m³/kg. The notable outlier is LU at 1.73 × 10⁻¹ to 2.67 m²acrop-eq/kg, but the WFLDB study uses ethanol from fermentation, which accounts for 2.56 m²acrop-eq/kg, and the remainder (1.10 × 10⁻¹ m²acrop-eq/kg) is similar to the impact reported here.

An alternative way of viewing impact is by contribution of input or emission type. Fig. 4 shows fractional contribution to impact of 1 kg

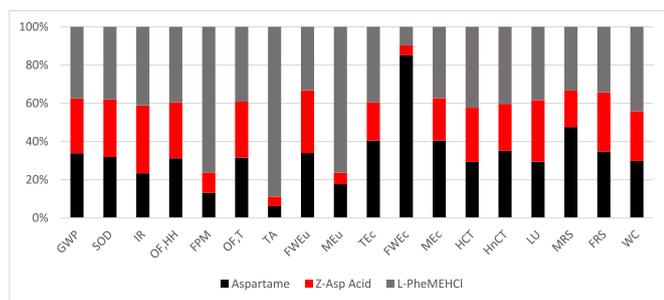


Fig. 3. Relative contribution to environmental impact of 1 kg aspartame from aspartame synthesis (black), Z-Asp acid production (red) and L-PheMEHCl production (grey). Key: GWP, global warming potential; SOD, stratospheric ozone depletion; IR, ionizing radiation; OF,HH, ozone formation, human health; FPM, fine particulate matter; OF,T, ozone formation, terrestrial; TA, terrestrial acidification; FWEu, freshwater eutrophication; MEu, marine eutrophication; TEC, terrestrial ecotoxicity; FWEc, freshwater ecotoxicity; MEC, marine ecotoxicity; HCT, human carcinogenic toxicity; HnCT, human non-carcinogenic toxicity; LU, land use; MRS, mineral resource scarcity; FRS, fossil resource scarcity; WC, water consumption. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 5

Absolute numerical impact data of 1 kg aspartame production. Data supports Fig. 3.

Impact category	Unit	Total	Aspartame	Z-Asp Acid	L-PheMEHCl
GWP	kg CO2 eq	29.25	9.91	8.37	10.96
SOD	kg CFC11 eq	1.06 × 10 ⁻⁵	3.40 × 10 ⁻⁶	3.20 × 10 ⁻⁶	4.05 × 10 ⁻⁶
IR	kBq Co-60 eq	1.09	2.56 × 10 ⁻¹	3.89 × 10 ⁻¹	4.49 × 10 ⁻¹
OF,HH	kg NOx eq	5.66 × 10 ⁻²	1.77 × 10 ⁻²	1.66 × 10 ⁻²	2.23 × 10 ⁻²
FPM	kg PM2.5 eq	1.26 × 10 ⁻¹	1.66 × 10 ⁻²	1.33 × 10 ⁻²	9.56 × 10 ⁻²
OF,T	kg NOx eq	5.93 × 10 ⁻²	1.87 × 10 ⁻²	1.74 × 10 ⁻²	2.32 × 10 ⁻²
TA	kg SO2 eq	7.68 × 10 ⁻¹	4.74 × 10 ⁻²	3.85 × 10 ⁻²	6.83 × 10 ⁻¹
FWEu	kg P eq	1.16 × 10 ⁻²	3.96 × 10 ⁻³	3.82 × 10 ⁻³	3.87 × 10 ⁻³
MEu	kg N eq	2.55 × 10 ⁻³	4.52 × 10 ⁻⁴	1.55 × 10 ⁻⁴	1.95 × 10 ⁻³
TEc	kg 1,4-DCB	1.24 × 10 ²	50.45	25.00	49.01
FWEc	kg 1,4-DCB	5.87	5.00	3.06 × 10 ⁻¹	5.67 × 10 ⁻¹
MEc	kg 1,4-DCB	1.65	6.68 × 10 ⁻¹	3.65 × 10 ⁻¹	6.13 × 10 ⁻¹
HCT	kg 1,4-DCB	1.18	3.48 × 10 ⁻¹	3.35 × 10 ⁻¹	5.01 × 10 ⁻¹
HnCT	kg 1,4-DCB	24.05	8.45	5.91	9.69
LU	m2a crop eq	5.87 × 10 ⁻¹	1.73 × 10 ⁻¹	1.89 × 10 ⁻¹	2.25 × 10 ⁻¹
MRS	kg Cu eq	9.98 × 10 ⁻²	4.75 × 10 ⁻²	1.90 × 10 ⁻²	3.33 × 10 ⁻²
FRS	kg oil eq	12.18	4.24	3.76	4.18
WC	m3	4.90 × 10 ⁻¹	1.46 × 10 ⁻¹	1.28 × 10 ⁻¹	2.16 × 10 ⁻¹

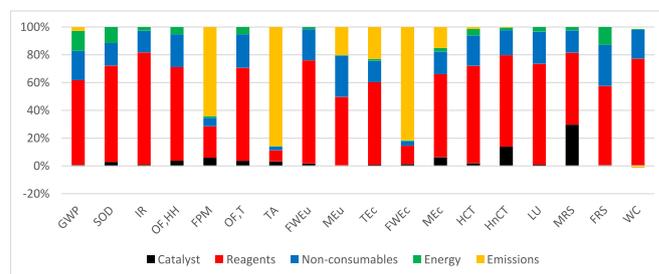


Fig. 4. Relative impacts for 1 kg aspartame production for each type of input or emission. Groupings shown are catalysts (black), reagents (red), non-consumables (blue), energy (green) and emissions (yellow). Impact categories defined in Fig. 3. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

aspartame from inputs from all production processes (i.e., aggregating those for aspartame, L-PheMEHCl and Z-Asp acid), such as catalysts (black), reagents (red), non-consumables (blue), and energy (green), and emissions (yellow). Supporting numerical data are given in Supplementary Material, Table S14. In this context, “non-consumables” are any materials which are not directly consumed by a reaction (as opposed to reagents which are directly consumed) and include solvents and resins. Technically, catalysts are also non-consumables, but are reported separately because they were found to be important for sensitivity in environmental impact and the effect of their consumption is explored separately (Section 5.1). The results show that reagents cause the most impact on average across all categories (57.1%), followed by non-consumables (18.2%) and emissions (16.3%). Catalysts contribute relatively little to net impact with an average of 4.4%. The results

indicate that optimization of reagent consumption is a good area to focus on for impact reduction.

Fig. 5 shows relative contribution to environmental impact of 1 kg neotame from Z-Asp acid (red), L-PheMEHCl (grey), aspartame (black) and the neotame synthesis step (green). Numerical data for absolute impact are given in Table 6. For GWP, net impacts are 43.42 kgCO₂-eq/kg. For LU, net impact is 1.08 m²acrop-eq/kg, for WC it is 5.54 × 10⁻¹ m³/kg, and MRS it is 2.06 kgCu-eq/kg. Across the impact categories neotame production accounts for an average of 63.1% of net impact, aspartame for 11.5%, Z-Asp acid for 8.3% and L-PheMEHCl 17.1%. In this instance, the neotame synthesis step contributes most impact across all impact categories, except for MEu and WC.

Fig. 6 shows fractional contribution to impact of 1 kg neotame from inputs such as platinum used only in the neotame synthesis step (black), all other catalysts (grey), reagents (red), non-consumables (blue), and energy (green), and emissions (yellow). The color coding is the same as Fig. 4 to aid in comparison. Numerical data are given in Supplementary Information, Table S15. The results show that impact is dominated by platinum consumption, accounting for an average of 57.9% impact across all categories. In terms of GWP, platinum contributes 15.71 out of 43.42 kgCO₂-eq/kg (36.2%). For LU it is 5.06 × 10⁻¹ out of 1.08 m²acrop-eq/kg (46.8%), MRS 1.97 out of 2.06 kgCu-eq/kg (95.7%), and WC 8.83 × 10⁻¹ out of 5.54 × 10⁻¹ m³/kg (15.9%). Due to this dominance of platinum, sensitivity to change in platinum recovery is explored in Section 5.1.

5. Discussion

5.1. Sensitivity to parameter change

The results showed that for aspartame, reagents were the main source of impact, and for neotame it was catalysts. However, this does not show how sensitive the results might be to variability in resource consumption. Therefore, several scenarios explore the sensitivity of the results to defined changes in process parameters. Each scenario is explored separately within its own sub-section, and supporting numerical data are given in Supplementary Material, Tables S16–S20, and further referenced in each scenario.

5.1.1. Scenario 1: recovery rates

Materials and heat energy consumed within the production process were subject to recovery rates (Fig. 2 and outlined in Section 2). Where possible these were derived from literature, but some by necessity were estimated. Nonetheless, none of the rates found were for material recovery specifically from aspartame or neotame production processes, and there may be variability in realistically achievable recovery rates. Therefore, a change of ±10% was explored for all material and heat recovery rates (or 100% recovery if assumed rate was already ≥90%). In addition, because change in recovery rate is linked to net resource consumption, this scenario is in effect also exploring sensitivity to

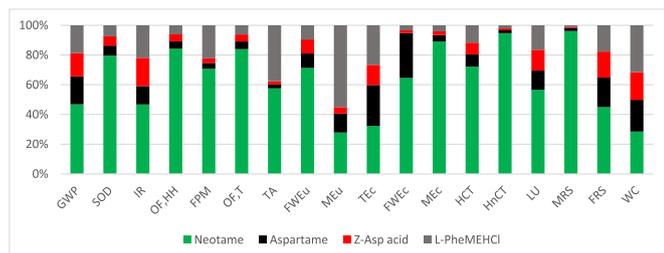


Fig. 5. Relative contribution to environmental impact of 1 kg neotame from neotame synthesis (green), aspartame synthesis (black), Z-Asp acid production (red) and L-PheMEHCl production (grey). Impact categories defined in Fig. 3. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 6

Absolute numerical impact data of 1 kg neotame production. Data supports Fig. 5. Impact categories defined in Fig. 3.

Impact category	Unit	Total	Neotame	Aspartame	Z-Asp Acid	L-PheMEHCl
GWP	kg CO ₂ eq	43.42	19.63	8.07	6.81	8.92
SOD	kg CFC11 eq	4.06	3.19 × 10 ⁻⁵	2.77 × 10 ⁻⁶	2.60 × 10 ⁻⁶	3.29 × 10 ⁻⁶
IR	kBq Co-60 eq	1.64	7.54 × 10 ⁻¹	2.08 × 10 ⁻¹	3.16 × 10 ⁻¹	3.66 × 10 ⁻¹
OF,HH	kg NOx eq	2.83	2.37 × 10 ⁻¹	1.44 × 10 ⁻²	1.35 × 10 ⁻²	1.82 × 10 ⁻²
FPM	kg PM2.5 eq	3.44	2.42 × 10 ⁻¹	1.35 × 10 ⁻²	1.09 × 10 ⁻²	7.78 × 10 ⁻²
OF,T	kg NOx eq	2.91	2.43 × 10 ⁻¹	1.52 × 10 ⁻²	1.41 × 10 ⁻²	1.89 × 10 ⁻²
TA	kg SO ₂ eq	1.46	8.30 × 10 ⁻¹	3.86 × 10 ⁻²	3.13 × 10 ⁻²	5.55 × 10 ⁻¹
FWEu	kg P eq	3.23	2.28 × 10 ⁻²	3.22 × 10 ⁻³	3.11 × 10 ⁻³	3.15 × 10 ⁻³
MEu	kg N eq	2.86	7.82 × 10 ⁻⁴	3.67 × 10 ⁻⁴	1.26 × 10 ⁻⁴	1.58 × 10 ⁻³
TEc	kg 1,4-DCB	1.48 × 10 ²	46.91	41.05	20.34	39.88
FWEc	kg 1,4-DCB	13.28	8.50	4.07	2.48 × 10 ⁻¹	4.62 × 10 ⁻¹
MEc	kg 1,4-DCB	11.90	10.56	5.43 × 10 ⁻¹	2.97 × 10 ⁻¹	4.77 × 10 ⁻¹
HCT	kg 1,4-DCB	3.36	2.40	2.83 × 10 ⁻¹	2.72 × 10 ⁻¹	4.08 × 10 ⁻¹
HnCT	kg 1,4-DCB	3.63 × 10 ²	3.43 × 10 ²	6.88	4.81	7.88
LU	m ² a crop eq	1.08	6.04 × 10 ⁻¹	1.41 × 10 ⁻¹	1.54 × 10 ⁻¹	1.83 × 10 ⁻¹
MRS	kg Cu eq	2.06	1.98	3.86 × 10 ⁻²	1.55 × 10 ⁻²	2.71 × 10 ⁻²
FRS	kg oil eq	17.53	7.62	3.45	3.06	3.40
WC	m ³	5.54 × 10 ⁻¹	1.55 × 10 ⁻¹	1.19 × 10 ⁻¹	1.04 × 10 ⁻¹	1.76 × 10 ⁻¹

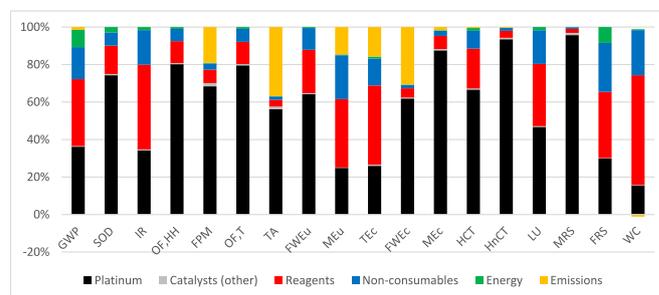


Fig. 6. Relative impacts for 1 kg neotame production for each type of input or emission. Groupings shown are platinum (black), all other catalysts (grey), reagents (red), non-consumables (blue), energy (green), and emissions (yellow). Impact categories defined in Fig. 3. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

resource consumption. The effect of change in recovery rates was explored per discrete input groups: catalysts, non-consumables, reagents, heat energy, and finally for all together.

Fig. 7 shows relative change in environmental impact of 1 kg aspartame, across all impact categories, for change in recovery rates of materials and heat energy. Lower bound (L) shown for all rates (black), catalysts (grey), heat energy (red), non-consumables (blue), and reagents (green), and upper bound (U) for all rates (yellow). Supporting numerical data are given in Supplementary Material, Table S16. The results show least sensitivity to reduction in reagent and heat energy recovery rates, with an average increase in impact of 2.9% and 2.1% respectively across all categories. In contrast, results are most sensitive to reduction in catalyst recovery rate (21.8% increase) and non-consumables recovery rate (14.9% increase). If all recovery rates are reduced to the lowest bound, environmental impact increases by an average of 42.2%. MRS is most sensitive to changes in catalyst recovery rates, highlighting the impact of palladium and nickel production. In contrast, increasing recovery rates to the upper bound results in an average impact reduction of 23.3%. This demonstrates that, with 13 out of 34 recovery rates already above 90%, not all rates can be increased by 10%, resulting in a skew towards increase in environmental impact with change in recovery rate.

Fig. 8 shows relative change in environmental impact of 1 kg neotame, across all impact categories, for change in recovery rate, and electrical energy and resins consumption. Lower bound (L) shown for all recovery rates (black), platinum (grey), heat energy (red), non-consumables (blue), and reagents (green), and upper bound (U) for all rates (yellow) and platinum (purple). Supporting numerical data are given in Supplementary Material, Table S17. In this instance, sensitivity is dominated by platinum recovery rate change with 289.4% increase in impact at the lower bound, and 57.9% decrease at the upper bound (+2% increase in recovery rate from baseline). This compares with a lower bound change of 292.7% for all recovery rates together. In isolation, assuming lower bounds for reagents causes a 2.9% increase in impact, 1.1% for heat energy, and 8.8% for non-consumables. This highlights the need to optimize platinum recovery above all others.

5.1.2. Scenario 2: electrical energy consumption

For baseline results, electrical energy consumption was estimated based upon mass of materials moved when stirring or pumping. However, it is inevitable that there are more demands for electrical energy within a production process. It was also found to be lower than that reported in the aspartame model from the WFLDB (Section 3.5). Therefore, a scenario explored the effect of an increase by 2-orders of magnitude in electrical energy consumption, making it well in excess of that used in the WFLDB model.

Fig. 9 shows relative change in environmental impact of 1 kg aspartame (black) and 1 kg neotame (red), across all impact categories, for increase by 2-orders of magnitude in electrical energy consumption.

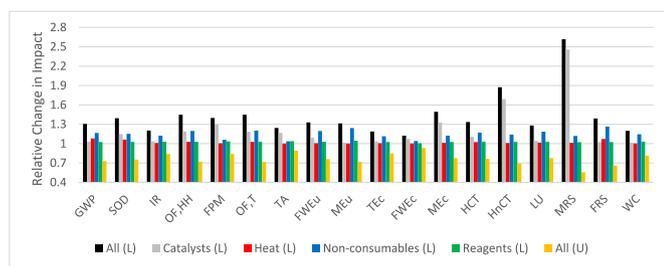


Fig. 7. Relative change of environmental impact of 1 kg aspartame to variation in recovery rates from lowest bound (L) for all rates (black), catalysts (grey), heat energy (red), non-consumables (blue), reagents (green), and upper bound (U) for all rates (yellow). Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

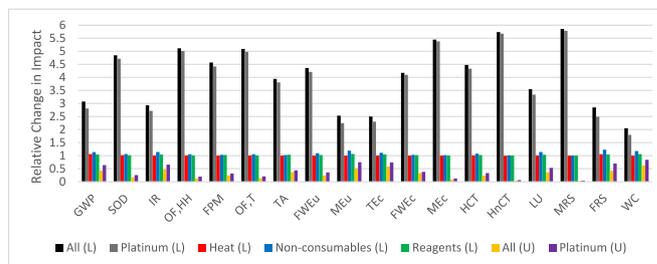


Fig. 8. Relative change of environmental impact of 1 kg neotame to variation in recovery rates from lower bound (L) for all rates (black), platinum only (grey), heat energy (red), non-consumables (blue), reagents (green), and upper bound (U) rates (yellow), and platinum only (purple). Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

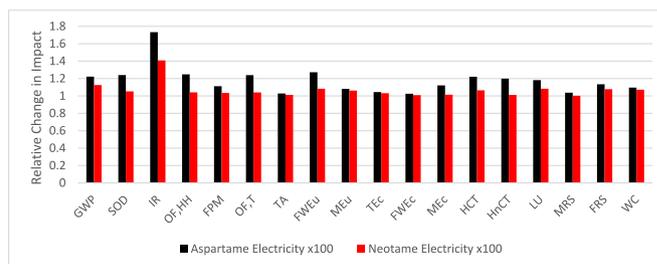


Fig. 9. Relative change of environmental impact of 1 kg aspartame (black) and 1 kg neotame (red) to increase by 2-orders of magnitude electrical energy consumption. Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Supporting numerical data are given in Supplementary Material, Tables S16 and S17. Increase in electrical energy consumption by 2-orders of magnitude leads to an average increase in impact of 18.0% for aspartame, and an average increase of 6.8% for neotame. For both NNS, the largest increase for IR at 73.3% for aspartame and 40.9% for neotame. Across all impact categories, aspartame is shown to be more sensitive to change in electrical energy consumption than neotame. However, net change is lower than might be expected from an increase by 2-orders of magnitude, demonstrating a relatively low sensitivity to electrical energy consumption when compared to materials, in particular platinum used for neotame production. For completeness, data for absolute impact change for both aspartame and neotame due to different step changes in electrical energy consumption are also given in Supplementary Material, Table S18.

5.1.3. Scenario 3: resin consumption

For baseline results, consumption of the D-PheME racemization resin was omitted. Therefore, in this scenario, consumption of resin in racemization of D-PheME to L-PheME was modelled using a proxy anionic exchange resin from the Ecoinvent database. No data for quantity used per mol of D-PheME, nor recovery rates were specified in Mirviss et al. (1990) for a single resin. Therefore, as per Mirviss et al. (1990, p657), a 1:2 mass ratio of resin to D-PheME (itself approx. half of the final product mass) as given for one resin, and a 25% recovery rate (which is a cautious minimum derived from the quote “the [resin] could be recycled 4 times without any loss in activity”) for another resin. Net consumption of resin is modelled as 187.5 g per 1 kg L-PheMEHCl.

Fig. 10 shows relative change in environmental impact of 1 kg aspartame (black) and 1 kg neotame (red), across all impact categories, for inclusion of D-PheME racemization resin consumption in modelling. Supporting numerical data are given in Supplementary Material,

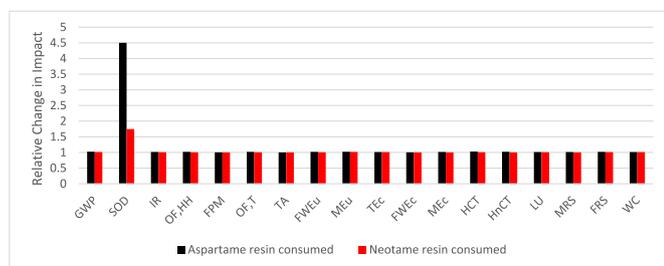


Fig. 10. Relative change of environmental impact of 1 kg aspartame (black) and 1 kg neotame (red) to inclusion of racemization resin consumption within impact calculations. Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Tables S16 and S17. The results show that aspartame is most sensitive to inclusion of resin consumption. This is particularly of note for SOD, for which aspartame shows a 450.1% increase in impact, and neotame a 74.7% increase. When omitting SOD, the average increase in impact across all impact categories is 1.5% for aspartame and 0.6% for neotame. The larger increase in SOD is due to trichloromethane production for the anionic resin in the Ecoinvent database. This highlights the need for further information regarding the specific resin used for racemization of D-PheME to L-PheME.

5.1.4. Scenario 4: waste treatment processes

For baseline results, it was assumed that materials which were not recovered and re-used, were emitted to the environment unchanged. The emission caused environmental impact through the attributes of those materials. However, it is likely that different materials will be treated prior to any emission to the environment. Therefore, in this scenario, all materials emitted (other than CO₂ and N₂) are subject to either hazardous waste disposal by incineration, or by wastewater treatment plant. The former is similar to the approach adopted by Huber et al. (2022), and the latter by the aspartame model in the WFLDB. For 1 kg aspartame, a total of 13.04 kg materials are treated, and for 1 kg neotame, it is 12.83 kg. It should be noted that water is a significant contributor to waste mass, but that both Ecoinvent process models used also assume a water fraction in the net mass.

Fig. 11 shows the effect of different waste disposal methods for unrecovered materials from, separately, 1 kg aspartame and 1 kg neotame production. Hazardous waste disposal shown for aspartame (black) and neotame (red), and wastewater treatment plant (WWTP) for aspartame (blue) and neotame (green). Supporting data are given in Supplementary Material, Table S19. The results show that for aspartame, hazardous waste treatment causes an average increase across all impact categories of 40.8%, and for neotame an increase of 15.8%. However, there are notable increases in GWP, SOD, FWEu, and HCT associated with

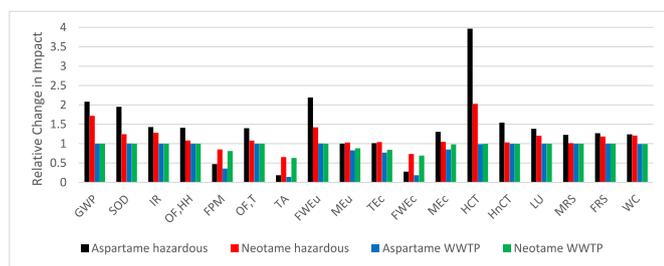


Fig. 11. Relative change of environmental impact due to different waste treatment methods for 1 kg aspartame and 1 kg neotame. Hazardous waste disposal shown for aspartame (black) and neotame (red), and WWTP disposal for aspartame (blue) and neotame (green). Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

incineration of hazardous wastes. In contrast, disposal of wastes by WWTP results in an average decrease of 16.0% across all impact categories for aspartame, and 6.5% for neotame. The results show that more specific information regarding the particular disposal methods used during production processes of individual materials will enable more accurate modelling of environmental impact.

5.1.5. Scenario 5: neotame proxy models

When modelling neotame production, a production route for 3,3-dimethyl butyraldehyde could not be found. Therefore, the baseline results were generated using cyclohexanol as a proxy. For this scenario, alternative proxies were chosen from the Ecoinvent database based upon similarity to 3,3-dimethyl butyraldehyde either by structure, number of atoms, or active groups: 2-methyl-1-butanol, 2,3-methylbutane, 3-methyl-1-butyl acetate, and benzaldehyde.

Fig. 12 shows relative change in environmental impact of 1 kg neotame using an alternative proxy for cyclohexanol in place of 3,3-dimethyl butyraldehyde: 2-methyl-1-butanol (black), 2,3-methylbutane (red), 3-methyl-1-butyl acetate (blue), and benzaldehyde (green). Supporting data are given in Supplementary Material, Table S20. Average relative change across all impact categories is 0.2% for 2-methyl-1-butanol, -1.1% for 2,3-methylbutane, 0.4% for 3-methyl-1-butyl acetate, and 0.1% for benzaldehyde. Sensitivity due to proxy change is less than that for recovery rate change of non-consumables and reagents, and much less than sensitivity to platinum catalyst recovery rate, as shown in Fig. 8. This demonstrates that further work is required to understand the environmental impact due to 3,3-dimethyl butyraldehyde, but not at the expense of understanding impacts due to other materials within the production process.

5.2. Sensitivity to uncertainty

The scenarios in Section 5.1 demonstrated sensitivity of baseline impact results to defined and uniform changes in foreground process parameters, i.e., they are all either at the upper or lower bound simultaneously. In this section, the effect of wider uncertainty within the process model is explored. In this instance, uncertainty is modelled using Monte Carlo simulation of parameter change over 5000 calculation iterations: the process parameters are free to vary randomly between the upper and lower bounds. The results are reported both in terms of mean of the Monte Carlo simulation and relative standard deviation (RSD). Furthermore, results are reported separately for background process uncertainty (i.e., process parameters used in this study for baseline results are fixed), and both foreground and background process uncertainty together. Uncertainty of foreground data is due to recovery rates (given in Supplementary Materials, Table S9), which are modelled as having a uniform distribution between ±10% bounds (or up to 100% if assumed rate is already ≥90%). Table 7 shows the results for aspartame

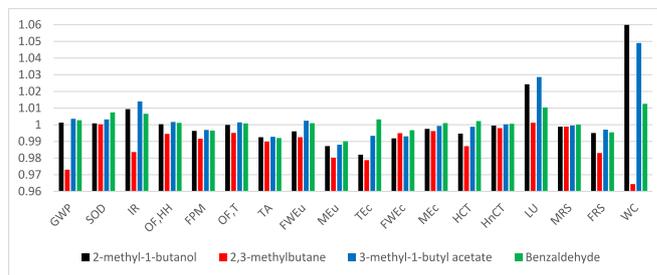


Fig. 12. Relative change of environmental impact of 1 kg neotame to different waste proxy materials for 3,3-dimethyl butyraldehyde: 2-methyl-1-butanol (black); 2,3-methylbutane (red); 3-methyl-1-butyl acetate (blue); and benzaldehyde (green). Impact categories defined in Fig. 3. Baseline impact results equal 1. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 7

Sensitivity of results to uncertainty within LCI, excluding recovery rates, for 1 kg neotame and 1 kg aspartame. Impact categories defined in Fig. 3.

Impact category	Unit	Neotame average	Neotame RSD	Aspartame average	Aspartame RSD
GWP	kgCO ₂ -eq	43.43	5.75	29.25	4.05
SOD	kgCFC11-eq	4.05 × 10 ⁻⁵	19.85	1.07 × 10 ⁻⁵	10.68
IR	kBqCo-60-eq	1.65	1.32 × 10 ²	1.11	1.41 × 10 ²
OF,HH	kgNOx-eq	2.83 × 10 ⁻¹	11.45	5.67 × 10 ⁻²	5.78
FPM	KgPM2.5-eq	3.44 × 10 ⁻¹	6.42	1.26 × 10 ⁻¹	2.23
OF,T	kgNOx-eq	2.91 × 10 ⁻¹	11.20	5.93 × 10 ⁻²	5.69
TA	kgSO ₂ -q	1.46	5.26	7.69 × 10 ⁻¹	8.15 × 10 ⁻¹
FWEu	kgP-eq	3.24 × 10 ⁻²	33.29	1.17 × 10 ⁻²	26.52
MEu	kgN-eq	2.86 × 10 ⁻³	7.24	2.5510 ⁻³	4.40
Tec	kg1,4-DCB	1.49 × 10 ²	25.01	1.24 × 10 ²	26.51
FWEc	kg1,4-DCB	13.32	20.14	5.88	7.65
MEc	kg1,4-DCB	11.96	27.93	1.65	34.52
HCT	kg1,4-DCB	3.36	1.56 × 10 ²	1.16	62.88
HnCT	kg1,4-DCB	3.58 × 10 ²	35.69	24.22	34.23
LU	m ² acrop-eq	1.08	14.91	5.86 × 10 ⁻¹	21.32
MRS	kg-Cu-eq	2.05	6.18	9.98 × 10 ⁻¹	20.13
FRS	kg-oil-eq	17.54	5.10	12.18	4.51
WC	m ³	5.72 × 10 ⁻¹	8.96 × 10 ²	4.58 × 10 ⁻¹	9.31 × 10 ²

and neotame if recovery rates are fixed (i.e., not used in the sensitivity analysis). Differences between the values reported in Table 7 and those in Tables 5 and 6 are due to the nature of the different calculations: Table 7 reports an average of multiple Monte Carlo calculation results from across process data uncertainty ranges, and Tables 5 and 6 report singular calculation results for baseline data. Table 8 shows the results if both background and variable recovery rates are modelled.

Results show that recovery rates have a more significant role in uncertainty for neotame than they do for aspartame. Likewise, there is a skew in the results for greater environmental impact because all recovery rates can be reduced by 10%, but only some may be increased by 10%. Large uncertainty of results for water consumption are due to net consumption only being a small part of total water flow through the system. Therefore, small changes in total input and output flows result in large change to net consumption.

5.3. Sucrose equivalence

Results shown in previous sections were in terms of 1 kg aspartame or 1 kg neotame. However, this does not reflect how NNSs are used in food and beverage products. Both NNSs are much sweeter than sugar: aspartame approx. 200-times, and neotame approx. 8000-times. Therefore, in this section, the relative impact of 5 g aspartame and 0.125 g neotame are compared with 1 kg sugar. These masses were not used for the results because relative sweetness is subjective, whereas the kilogram is a recognized SI unit. It should be noted that LCA system boundaries will be markedly different for agriculturally produced sugar and synthetically produced aspartame, or neotame. However, it is still informative to explore relative impact of delivering 1 kg sweetness equivalence (1 kg_{SE}).

Fig. 13 shows the relative impact of 1 kg_{SE} aspartame (black and red bars) and 1 kg_{SE} neotame (blue and green bars) compared with that of 1

Table 8

Sensitivity of results to uncertainty within LCI, including recovery rates. Impact categories defined in Fig. 3.

Impact category	Unit	Neotame average	Neotame RSD	Aspartame average	Aspartame RSD
GWP	kgCO ₂ -eq	74.52	38.27	29.87	8.60
SOD	kgCFC11-eq	9.99 × 10 ⁻⁵	58.62	1.14 × 10 ⁻⁵	12.78
IR	kBqCo-60-eq	2.82	1.57 × 10 ²	1.07	1.27 × 10 ²
OF,HH	kgNOx-eq	7.29 × 10 ⁻¹	55.90	6.15 × 10 ⁻²	11.28
FPM	KgPM2.5-eq	8.14 × 10 ⁻¹	51.05	1.40 × 10 ⁻¹	9.82
OF,T	kgNOx-eq	7.47 × 10 ⁻¹	55.68	6.44 × 10 ⁻²	11.29
TA	kgSO ₂ -q	3.08	46.79	8.19 × 10 ⁻¹	5.98
FWEu	kgP-eq	7.26 × 10 ⁻²	64.70	1.21 × 10 ⁻²	28.53
MEu	kgN-eq	4.24 × 10 ⁻³	32.83	2.57 × 10 ⁻³	12.76
Tec	kg1,4-DCB	2.23 × 10 ²	38.59	1.27 × 10 ²	26.50
FWEc	kg1,4-DCB	29.28	56.52	6.05	7.99
MEc	kg1,4-DCB	32.24	64.78	1.86	32.86
HCT	kg1,4-DCB	7.74	98.18	1.23	64.86
HnCT	kg1,4-DCB	1.04 × 10 ³	73.34	30.63	36.37
LU	m ² acrop-eq	2.08	44.91	6.01 × 10 ⁻¹	23.16
MRS	kg-Cu-eq	5.94	57.81	1.58 × 10 ⁻¹	34.30
FRS	kg-oil-eq	28.10	33.66	12.59	10.17
WC	m ³	6.66 × 10 ⁻¹	9.99 × 10 ²	4.24 × 10 ⁻¹	1.03 × 10 ³

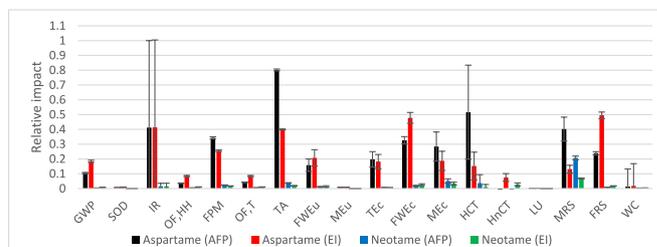


Fig. 13. Relative environmental impact of 1 kg sweetness equivalence of aspartame (black and red bars) and neotame (blue and green based) compared to 1 kg_{SE} of global mix of sugar from Agri-footprint 6.1 (AFP) and Ecoinvent 3.3 (EI) databases. Relative impact of 1 kg sugar equals 1. Impact categories defined in Fig. 3. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

kg sugar from the Agri-footprint 6.1 (AFP) and Ecoinvent 3.3 (EI) databases using a global mix of 80% sugar from cane and 20% from beet (ISO, 2020; OECD/FAO, 2021). Error bars are based upon standard deviation from the sensitivity analysis conducted in Table 7, and further reported in Supplementary Material, Table S21, alongside other supporting data. Results show that both aspartame and neotame have the potential to reduce environmental impact for a given level of sweetness compared with sugar. Impact is lower across all categories, however the large uncertainty in IR should be noted. Neotame has lower impact than aspartame, showing that any impact due to the extra neotame synthesis step is offset by increase in sweetness from 200- to 8000-times that of sugar. Also notable is the relative LU and WC, which is small for both aspartame and neotame, demonstrating the disconnect from growing crops to providing sweetness offered by these NNSs. In this regard, they have good potential for land sparing if they were to replace large quantities of added sugar in food and beverage markets. It is worth

noting that Agri-footprint HnCT comparison is negative for both NNSs. This is because HnCT impact of sugar in the Agri-footprint database is negative, indicating a net absorption of toxic materials during production. A cradle-to-grave LCA is required to understand the true, net HnCT comparison.

5.4. Functional use of NNSs

It is not always possible to replace added sugar directly with NNSs. In solid formulations, technical functions of added sugar, including hygroscopic control or mouth feel, must also be adjusted. One option is sugar alcohols (e.g., sorbitol) but there is little LCA data relating to these. The authors are aware of two LCAs of sorbitol (Akmalina, 2019; Moreno et al., 2020) and no others for other sugar alcohols. Reported GWP is between 2.20 kgCO₂-eq/kg_{sorbitol} and 5.09 kgCO₂-eq/kg_{sorbitol}. Sorbitol is made by hydrogenating glucose, which is derived from hydrolyzed corn starch, and any difference in impact depends on whether the starch undergoes hydrolysis using acid (1.56 kgCO₂-eq/kg_{glucose}) or enzymes (4.45 kgCO₂-eq/kg_{glucose}).

Replacing 1 kg added sugar in a solid formulation requires approx. 5 g aspartame and 995 g sorbitol, to give both sweet taste and technical function. Aspartame and sorbitol combined like this create at least 2.34 kgCO₂-eq/kg. Likewise, 0.125 g neotame used alongside 999.875 g sorbitol creates an impact of at least 2.21 kgCO₂-eq/kg. This compares to a global mix of sugar of 1.39 kgCO₂-eq/kg as per the Agri-footprint 6.1 database. This highlights that more study is required to understand environmental ramifications of NNSs use in formulations, and more widely within whole diets, to best understand entire life cycle impacts of producing and consuming NNSs.

5.5. Uncertainty within data

Variation in the LCA results reported here demonstrate sensitivity of calculated impact to key parameters. For neotame, the recovery rate of platinum catalyst dominates the environmental impact calculation, whereas for aspartame, it tends to be a combination of catalysts and non-consumables. Therefore, net use of materials is an area that would benefit from greater collaboration with industry to understand real-world consumption rates as opposed to those based upon estimated data.

Another significant unknown in the results was energy required for different processes. For instance, in [Supplementary Material Tables S2, S4 and S8](#), data show that under certain circumstances processes might be exothermic, i.e., net energy producing. While this might be the case for an individual reaction, it does not guarantee that the same reaction in an industrial setting will allow a factory to be self-supporting for energy needs. Such data can only be understood through collaboration with industrial chemical producers.

This highlights the challenges of conducting an LCA of industrially manufactured chemicals using data derived from patents and other literature. For instance, it was assumed that reaction by-products and unrecovered materials were emitted to the environment unchanged. In reality some form of waste treatment would be applied (as explored in Section 5.1), and collaboration with industry would allow better definition of the quantities and forms of materials either treated or emitted. Moreover, focusing only on reactions does little to understand additional resource requirements of the factory in which production takes place.

There are legitimate concerns regarding confidentiality and intellectual property of any industrial process, and these can hamper collaboration. However, using factory scale aggregated data can simultaneously help ensure confidentiality of process steps, and provide more accurate production data for an LCA. Indeed, the level of process detail given in this report is only necessary to highlight assumptions used in this study and does not need to be disclosed if factory level data were presented instead.

5.6. Limitations and further research

The LCA presented is for aspartame and neotame production, and multiple sources of uncertainty in data have been highlighted. Further research is needed to reduce these uncertainties. For example, reduced yields, unless otherwise stated, were assumed to be due to unreacted reagents, and not through creation of side-products. This is unlikely to be the case, and to account for this effectively, more knowledge is required about potential side-products. Likewise, materials quantities were derived from literature which reports experimental production processes, and not large-scale, optimized industrial processes. Therefore, material use may not be optimized, leading to a potential overestimate in this study. Neither set of information was available for this study and is an area for future investigation, preferably in collaboration with industry.

The LCA does not include use of the two NNSs in foods or beverages. To better understand whole life cycle impacts, this work needs to be expanded to include whole foodstuffs, their consumption in diets, and waste disposal after consumption. In particular, sucrose equivalencies used for comparison to sugar are only indicative, and quantities used in food vary depending on the nature of the other ingredients, for instance flavor profiles. Hence, it is unlikely that neotame will always be used in a quantity exactly 8000-times less than sugar in a formulation. Therefore, to truly understand the environmental impact of using NNSs within the context of food and drink, real formulations need to be studied. This is another area for future research.

This study is also an attributional LCA, in which impacts for producing the NNSs are reported in isolation. Given that NNSs specifically replace added sugar in formulations, consequences of making this change need to be explored: a consequential LCA. One area for focus is the potential to spare land by using chemically derived NNSs. For instance, 1 kg_{SE} aspartame causes 2.93×10^{-3} m²acrop-eq and 1kg_{SE} neotame 1.35×10^{-4} m²acrop-eq, compared to 1.39 m²acrop-eq for 1 kg_{SE} sugar. This indicates the potential to spare land for other purposes, with associated biodiversity benefits, but implications of this need further study.

6. Conclusions

There is significant interest in the potential for NNSs to replace the sweet taste of added sugar in diets. However, it is not only important to know the health ramifications of replacing added sugar; the environmental and wider sustainability ramifications should also be understood. While there is much research relating to environmental impact of sugar, there is very little for NNSs. Most NNS related research has focused on stevia-based sweeteners, and there is relatively little on other major sweeteners. This study helps fill that gap by presenting the first LCA of chemically derived aspartame, and the first of any kind for neotame.

Environmental life cycle assessment of producing 1 kg of aspartame and neotame has been presented in this study. The results showed that in terms of replacing the sweetness of sugar, both NNSs have potential to create significantly less environmental impact across multiple impact categories. In particular, the extra perceived sweetness of neotame compared with aspartame offsets any further environmental impacts incurred from additional synthesis steps to produce it from aspartame. However, there is uncertainty regarding life cycle data, which would benefit from industrial collaboration and access to data for the manufacturing processes. Accuracy of data relating to recovery rates of catalysts and non-consumables used in reactions, and holistic energy consumption, needs improving. Nonetheless, this study helps build an evidence base from which wider dietary studies may be conducted, representative of commonly used NNSs.

This study was for cradle-to-factory-gate, and the importance of understanding environmental impact of NNS use in products and diets is highlighted. When replacing added sugar in solid formulations, the

impact of other necessary ingredients (e.g., sugar alcohols), also needs to be considered. This highlights the need to not only to understand production of NNSs, but also the context in which they are used, and potential health benefits of consuming low added sugar products. These are all areas for future exploration of the environmental impact of both aspartame and neotame, and other NNSs.

CRedit authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jclepro.2023.138854>.

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