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Development of a food composition database for the estimation of dietary S-methyl cysteine sulfoxide from vegetables

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ABSTRACT

A food composition database estimating S-methyl cysteine sulfoxide (SMCSO) was created following a systematic literature search. SMCSO data (705 entries) from 19 vegetables were summarised: brassicas (n = 10) and alliums (n = 9). The highest SMCSO in brassicas was reported in Brussels sprouts (median [range]: 318 [68–420] mg/100 g fresh weight (FW)) whilst the lowest was in radish (19 [4–45] mg/100 g FW). Brussels sprouts were almost twice as concentrated in SMCSO as cauliflower, followed by cabbage, kale, broccoli, kohlrabi, swede, Chinese cabbage, and turnips. The alliums highest in SMCSO were Chinese chives (271 [185–413] mg/100 g FW) followed by rakkyo and garlic, with substantially less found in shallots, onion, and leek. Literature reporting SMCSO content in food is sparse. Further research is required to quantify SMCSO in commercially available vegetables and other foods, in order to update and expand this database for application to large populations and future intervention studies.

1. Introduction

Higher intake of vegetables is associated with a lower risk of non-communicable diseases, such as cardiovascular disease (CVD), cancer, and respiratory disease, as well as all-cause mortality (Aune et al., 2017; Wang et al., 2021). Brassica vegetables, also known as cruciferous (e.g., broccoli, cabbage, cauliflower, kale) and alliums (e.g., garlic, onion, leek) appear to offer the greatest cardio-protective benefits (Blekkenhorst, Bondonno, et al., 2017; Zurbau et al., 2020). Both brassica and allium vegetables have also been studied extensively for their anti-cancer, antimicrobial, and anti-diabetic potential, in addition to their anti-inflammatory, antioxidant, neuro-protective, immunological and bone stengthening benefits (Blekkenhorst, Hodgson, et al., 2017; S. Petropoulos et al., 2017; Zeng et al., 2017). Whilst these vegetables contain vitamins, minerals, fibres, and polyphenols, they are known to be particularly rich in sulfur-containing compounds, such as

Abbreviations: AGRICOLA, AGRICultrual OnLine Access; ASCO, S-alkenyl cysteine sulfoxide; DW, dry weight; EMBASE, Excerpta Medica dataBASE; FW, fresh weight; GSLs, glucosinolates; HPLC, high-performance liquid chromatography; ID, identification; IQR, interquartile range; NA, not available; SMCSO, S-methyl cysteine sulfoxide; SD, standard deviation; SEM, standard error of the mean.

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glucosinolates (GSLs) (e.g., glucoraphanin) and cysteine sulfoxides (e.g., S-methyl cysteine sulfoxide; SMCSO, also referred to as methiin) (Hill et al., 2022). Evidence suggests the relative abundance of sulfur-containing compounds within brassica and alliums may partly explain their disease modifying potential (Hill et al., 2022).

Most of the research on the benefits of sulfur-based compounds in brassica vegetables is heavily focused on GSLs (Edmands et al., 2013; Petropoulos et al., 2017a). However, these vegetables contain a substantially higher concentration of SMCSO than GSLs at approximately 1–4% dry weight compared to 0.1–0.4% (Mae et al., 1971; Marks et al., 1992). SMCSO was first identified in brassica vegetables (i.e., turnips, cabbage, cauliflower, and kale) in the 1950's (Morris & Thompson, 1956; Synge & Wood, 1956). High concentrations of SMCSO are found in plants of the *Brassicaceae* family (Edmands et al., 2013), whereas lower amounts have been identified within plants of the *Alliaceae* (i.e, alliums) (Carson & Wong, 1961). SMCSO has also been identified in other plant foods such as the *Astragalus* and *Phaseolus* genera of the *Fabaceae* family (i.e., legumes and beans) (Edmands et al., 2013). Although SMCSO has been identified in *Astragalus,* it has not been quantified (Dunnill, 1967). Additionally, early reports have suggested that SMCSO is found in common beans, however, the presence of analogues such as S-methyl cysteine (a non-sulfoxide form) have been mistakenly identified as SMCSO in beans (Giada, 1998).

Early agricultural research referred to SMCSO as 'kale anaemia factor' for its potential to cause haemolytic anaemia and subsequent death when large quantities of brassica (especially kale) were fed to ruminant livestock (Whittle et al., 1976). However, research using non-ruminant animal models suggests that SMCSO may provide anti-carcinogenic and cardiovascular benefits (Fujiwara et al., 1972; Komatsu et al., 1998; Kumari & Augusti, 2007). More recently, the ingestion and subsequent accumulation of SMCSO and its derivatives have been explored in men with early/suspected prostate cancer, observing that greater intake of SMCSO-rich foods (i.e., brassica vegetables) correlated with lower prostate cancer grading (Coode-Bate et al., 2019). Despite evidence indicating that SMCSO may have the potential for cardiometabolic health using animal models, this is yet to be well explored in humans (Edmands et al., 2013).

Researchers do not have a comprehensive food composition database readily available that details the SMCSO content in vegetables or other foods. Without a database, researchers are unable to adequately estimate the dietary intake of SMCSO and apply this to large population-based studies to assess associations of intake with health outcomes. Nor are researchers able to explore its potential effects within dietary intervention studies. Such a database will enable investigations of the associations and effects of SMCSO with disease risk and health outcomes. This project aimed to develop a food composition database to assess SMCSO levels reported in commonly consumed vegetables. We also explored factors impacting SMCSO variability of different vegetables.

2. Materials and methods

2.1. Development of the database

2.1.1. Search strategy/data collection

A comprehensive, systematic literature search was conducted to identify previously published data reporting the SMCSO content of vegetables and foods inclusive of all dates through to 16 July 2023. Due to the relatively low number of publications anticipated, we chose not to exclude publications prior to any particular year. Excerpta Medica dataBASE (EMBASE), Medline, AGRICultural OnLine Access (AGRICOLA), and the Commonwealth Agricultural Bureau Abstracts were the primary databases investigated. Key search terms incorporated synonyms for SMCSO as well as food composition, analysis, and individual vegetable names, applied across all-text (not just title and abstract) wherever possible (Supplementary Table 1). Grey literature and government agency reports were searched through the Web of Science, Google Scholar, and government websites for additional data. Furthermore, manual citation searching from publication lists was cross-checked. The total number of articles, and their sources, were recorded and imported into an Endnote X9 library (Thomas Reuters) and duplicates were removed.

2.1.2. Data evaluation and selection process

All citations were uploaded into Covidence software (Covidence Veritas Health Innovation, Melbourne, Australia) for the evaluation and selection process. The title and abstract of each article were reviewed independently by two authors (CRH and ELC). To meet the initial eligibility for a full-text review, the paper had to: i) report the SMCSO content in vegetable/s, herbs, spices, and/or any edible plant-based foods, and ii) be published in English. If either reviewer found an article was 'unclear' in meeting these criteria, (i.e., assessed as 'maybe' within Covidence), then the article progressed to full-text review. If an abstract did not discuss SMCSO (or any of our keywords) but it discussed foods and/or plants that could possibly contain SMCSO, then we deemed this to be 'unclear', and the article progressed for full-text review. Full-text articles were then assessed for eligibility independently by two authors (CRH and ELC), with a third author (LCB) introduced to make final decisions on any discrepancies. Articles were excluded if the SMCSO content was: i) unclear or not quantified, ii) not measured in the edible part of the vegetable/plant, or iii) harvested prior to typical human consumption. To maximise the number of articles, vegetables intended as fodder (e.g., kale, turnips, swedes) were included if they reported being grown under normal conditions (i.e., not experimentally manipulated). In the rare event of SMCSO levels being cited by other researchers (i.e., in reviews or discussions), we always obtained the original publication source for the raw data, so measurements were never extracted twice. The total number of articles at each step of the process, as well as their reasons for inclusion or exclusion, were recorded and documented as per Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Page et al., 2021). The final selected articles identified as meeting the set criteria were used to extract SMCSO data for the database.

2.1.3. Data compilation

Data were extracted into a Microsoft Excel (version 16) spreadsheet. The following was extracted: i) publication information (year of publication, author/s, country, and publication type); ii) vegetable information (common name, scientific name *[both as reported]*, cultivar *[if known]*, and cooking, preservation, country of growth, growing and/or storage methods *[if known]*; iii) sampling information (month, season, year of the sample *[if known],* use of any fertilisers/ additives, or other reported conditions, and whether it was direct or compiled data); iv) measurement information (the originally stated unit, and the conversion to mg/100 g for analyses), sample type (i.e., fresh or dry weight), value type, sample size, and analytical method/s used. When the country of growth was unclear, it was extracted as 'not reported'. Where results were provided in a graphical format, the corresponding author was contacted. If the raw numerical values were unavailable, the publication was subsequently excluded. When a publication reported results in dry weight (DW), yet provided moisture content (or DW%), we converted the value to fresh weight (FW). If there was no DW% provided within the publication, then a FW conversion was calculated based on the vegetables' moisture content sourced from already existing food composition databases for each country of growth (Supplementary Table 2). If the country of growth was unclear for the purpose of calculating FW, then the corresponding authors' country of affiliation was assumed as the country of growth. Conversions were also checked against DW%s within included publications and found to be highly comparable. Vegetable sources were sub-categorised as being from (i) market, (ii) retail/commercial (e.g., the supermarket or grown as a commercially-available source), (iii) producer/cultivator (e.g., collected directly from grower),

(iv) department, association or research institute (e.g., collected from a university department, Vegetable Growers Association or plant Research Institute), (v) other (e.g., wild), (vi) not reported, (vii) trial site (e.g., grown with minimal alteration in growing conditions), or (viii) experimental conditions (e.g., trial sites with clear manipulation during growth such as altered doses of stimulants/fertilizers/additives). If the sample size was unclear, it was recorded as n = 1. Lastly, when a sample was divided into various sections (i.e., inner/outer onion flesh, inner/outer cabbage leaves) we averaged the levels of SMCSO across all different edible sections unless otherwise indicated, so the given sample size was not overinflated.

2.2. Data aggregation and statistical methods

Due to the relatively small number of studies that have quantified SMCSO within various vegetables, attempts were made to maximise the number of entries whilst simultaneously maintaining accuracy and transparency. For example, ideally, the database would only include those vegetables strictly purchased through retail, and thus accessible to the retail consumer (i.e., supermarket purchases), however, this provided limited data. We, therefore, stratified results based on the source of sample (e.g., samples sourced from markets, retail/commercial, producers/cultivators, department/association/research institute) to determine if any differences exist between those available for human consumption and those intended for either animal feed and/or from a trial site. After exploring samples sourced from trial sites, we further stratified those grown under experimentally manipulated conditions (i.e., when the sample was intentionally manipulated during its growth period [addition of selenium, sulfur, nitrogen, etc]). Whilst remaining in the database, we excluded these from our main analysis as they were likely not representative of vegetables commonly available for human consumption. This small subset of experimentally manipulated samples included kale (n = 20 entries) and onion (n = 29 entries) **(Supplementary Table 3).** Growing methods were also stratified into the open air (e.g., open field, wild-grown) or undercover (e.g., glasshouse, greenhouse) for analysis when sufficient data was available. If a vegetable was exclusively animal forage (i.e., forage rape) it was reported separately. However, if sources/seeds could be purchased for home consumption (e.g., Maris Krestel kale - typically used for animal forage) it was included.

Whilst the database includes various cooking and/or preservation methods (e.g., boiled, blanched, microwaved, baked, sprouted, dried, juiced, crushed), this data should be interpreted with caution due to the wide variability in heating conditions (time, temperature, methodology, etc.) and lack of data for comparison. Our main analysis presents aggregated data from fresh, uncooked samples of ≥ 3 publications. All other data is provided separately as supplementary. Many values were not normally distributed; therefore, our descriptive statistics include the mean ± standard deviation (SD), median and interquartile range (IQR), minimum and maximum for each vegetable compiled from the total number of SMCSO reported values on that particular vegetable. Due to the relatively low number of publications quantifying SMCSO, our analysis is mainly descriptive. Nonetheless, we were able to assess the impact of several variables (growing/environmental conditions) upon SMCSO levels in three of our vegetables (onion, garlic, and kale) for which we had sufficient data. For this, mixed methods regression was performed using both unadjusted and publication identification (ID)-adjusted models and presented as mean and standard error of the mean (SEM). Publication ID was used in the adjusted model as we did not have adequate data to adjust for varying factors individually. Publication ID was applied as a random factor, for pseudo-representation of variation in country, year, methods of analysis, and other heterogenic factors. Our analyses used a combination of GraphPad PRISM (version 9), SPSS (version 26, SPSS Inc, Chicago, USA), and STATA (version 16, Statacorp, College Station, TX, USA). GraphPad PRISM (version 9) has provided all graphical displays for visual representations.

3. Results

3.1. Database overview

A flowchart of our systematic literature search is presented in Fig. 1.

The full database provides SMCSO values compiled from 78 publications published between 1956 –16 July 2023, from 17 countries (Supplementary Table 4). Corresponding authors of publications were predominantly from the USA (n = 15), Japan (n = 13), UK/Scotland (n = 12), and the Czech Republic (n = 10), representing 64% of the total included publications. The 78 publications provided 926 individual data entries (total sample size n = 4005), across a variety of predominantly brassica and allium vegetables. Most vegetables (73% of the total 926 entries) were grown in the northern hemisphere; mostly the UK (n = 140), the Czech Republic (n = 93), and Japan (n = 89). Four vegetables were reported in DW [vegetable, n = entries (sample size); Ethiopian cabbage, n = 1 (1); rape, n = 69 (392)]; aged garlic, n = 6 (25); and blackened onion, n = 6 (39); and were unable to be converted to FW, shown in Supplementary Table 5. The remaining 844 entries were either FW (n = 462) or able to be converted from DW to FW due to available moisture content data (n = 382). A small number of these entries [n = entries (sample size); n = 12 (17)] were from cooked or processed vegetables: blanched broccoli [n = 3 (3)], juiced and/or steamed cabbage [n = 2 (2)], blanched [n = 2 (2)] or dried [n = 1 (1)] hooker chives, cooked onion [n = 1 (1)], 72-hour radish sprouts [n = 1 (1)] and blackened garlic [n = 2 (7)] (Supplementary Table 6). After removing these data, 832 entries of fresh, uncooked and/or unprocessed vegetables remained. However, a number of these entries were reported from ≤2 publications (Supplementary Table 7) and, therefore, subsequently removed from the main analysis. Although containing only very small levels of SMCSO, some of these were alliums belonging to the subfamilies *Tulbaghioideae* and *Gilliesioideae*, often referred to as 'low odour' garlic, and native to South Africa and South America. The common and/or alternate names of the individual vegetables are also provided in Supplementary Table 8.

3.2. SMCSO content in vegetables

Vegetables that had sufficient data (i.e., reported by ≥3 publications) for descriptive analysis included allium (n = 9) and brassica (n = 10) and were derived from 15 different corresponding-author-affiliated countries, 64 publications with a total of 705 entries (total sample size n = 3076) (Supplementary Table 9). These vegetables were grown across ≥21 different countries, mostly in the Northern hemisphere (77%); UK (n = entries; n = 140), Czech Republic (n = 93), Japan (n = 89), Germany (n = 41), USA (n = 29), Korea (n = 22), Spain (n = 22), Canada (n = 20), Netherlands (n = 19), Indonesia (n = 17), New Zealand (n = 13), Scotland (n = 12), China (n = 11), Italy (n = 27), Argentina (n = 9), Ukraine (n = 6), Australia (n = 4), Vietnam (n = 3), France (n = 2), Belgium (n = 2), and Sweden (n = 2), with the remaining not reported (n = 121). Descriptive statistics on SMCSO levels reported within these fresh, uncooked and/or unprocessed vegetables, are presented in Table 1.

The median SMCSO content of each individual vegetable is displayed from the highest (Brussels sprouts) to the lowest (radish) in Fig. 2.

Brussels sprouts were almost twice as high in SMCSO when compared to cauliflower, followed by relatively even concentrations in cabbage, kale, broccoli, kohlrabi, and swede. Relatively low amounts were reported in Chinese cabbages, turnips, and even less in radishes. Of the allium vegetables, Chinese chives contained the highest median SMCSO followed by rakkyo. Both the common garlic and elephant garlics were similar in SMCSO content, and the remaining alliums (Welsh onion, shallot, onions, and leek) were the lowest of those measured. Interestingly, Chinese chives (*Allium tuberosum*) contained approximately five times more SMCSO than common chives (*Allium schoenprasum*) and blue chives (*Allium nutans*) (Supplementary Table 8)

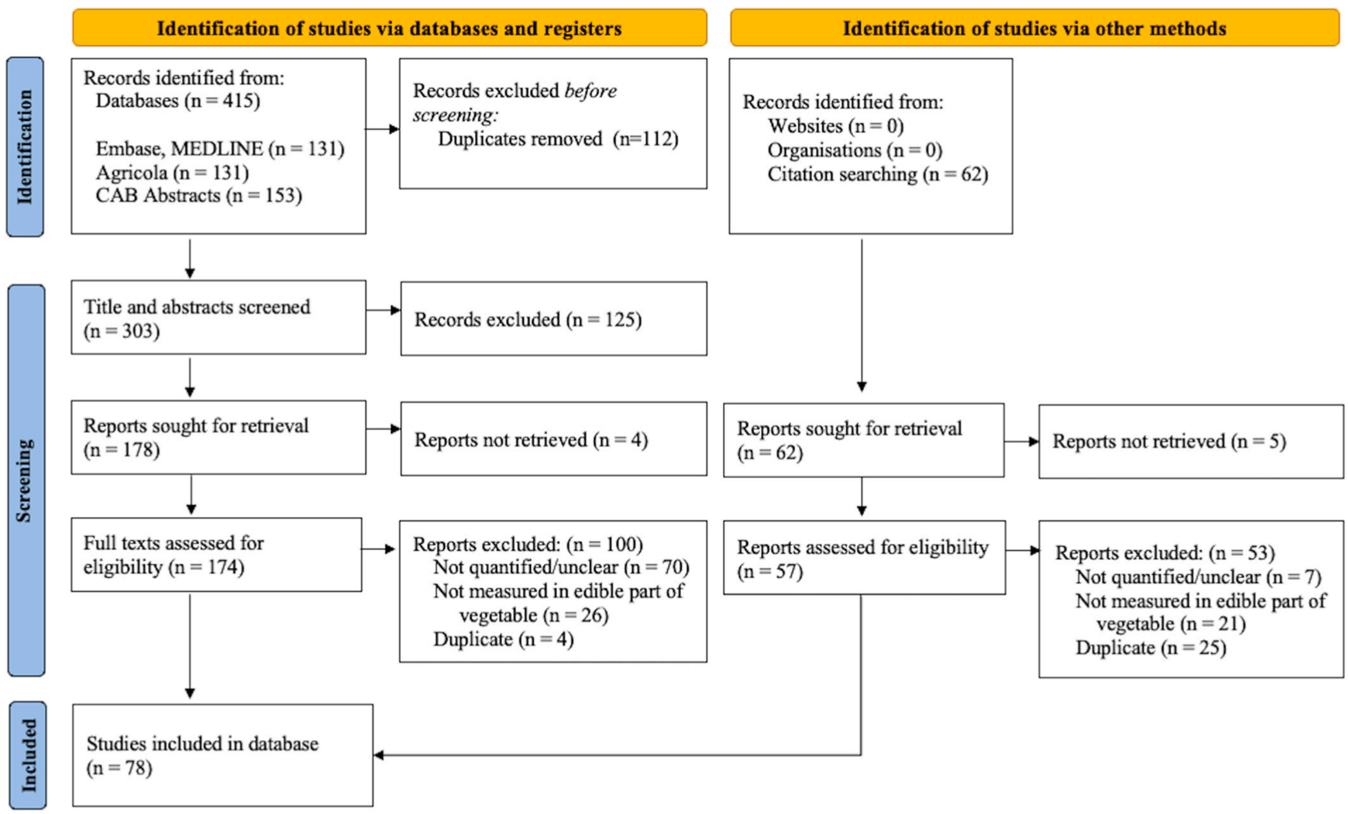

Fig. 1. PRISMA flow diagram.

Table 1
SMCSO content (mg/100 g FW) in uncooked, unprocessed vegetables.

Common vegetable name	Mean ± SD	Median (IQR)	Minimum -Maximum	Sample size[a]	Number of entries	Number of publications[b]	Number of countries sampled
Alliaceae							
Chives	57 ± 22	54 (33–80)	32–86	13	7	4	3[c]
Chinese chives	291 ± 69	271 (250–332)	185–413	34	12	5	1[c]
Elephant garlic	84 ± 31	89 (45–106)	43–126	9	7	4	3[c]
Garlic	107 ± 77	95 (57–145)	0–532	1118	175	22	9[c]
Leek	42 ± 55	20 (18–43)	4–231	33	17	9	6[c]
Onion	67 ± 76	24 (12–126)	1–292	963	158	33	12[c]
Rakkyo	159 ± 71	200 (82–211)	81–245	22	7	3	3
Shallot	34 ± 26	29 (22–43)	3–175	102	40	8	8[c]
Welsh Onion	40 ± 34	30 (12–73)	6–91	14	6	4	2[c]
Brassicaceae							
Broccoli	112 ± 70	96 (68–168)	0–208	40	15	9	5[c]
Brussels sprouts	269 ± 181	318[(NA)]	68–420	8	3	3	1[c]
Cabbage	102 ± 35	100 (80–124)	19–206	130	47	11	4[c]
- *White*	99 ± 31	97 (67–122)	49–154	58	21	4	2[c]
Cauliflower	152 ± 96	165 (56–240)	14–285	17	10	9	1[c]
Chinese cabbage	40 ± 10	40 (35–46)	17–56	11	11	4	2[c]
Kale	101 ± 44	96 (71–130)	19–373	335	127	8	4[c]
Kohlrabi	105 ± 32	96 (80–139)	80–149	5	4	4	1[c]
Radish	22 ± 12	19 (13–33)	4–45	37	16	7	5[c]
Swede	89 ± 32	91 (58–111)	42–165	131	28	5	2[c]
Turnip	36 ± 20	35 (21–44)	12–80	56	15	6	2[c]

[NA] not available. Interquartile range (IQR) unable to be calculated as only 3 entries available. FW, fresh weight; SD, standard deviation, SMCSO, S-methyl cysteine sulfoxide.
[a] assigned as 1 when the publication did not clearly state the sample size.
[b] data included only when ≥ 3 samples were available on a particular vegetable
[c] ≥1 publication had the country of growth not reported

had less than half of that found in common chives.

Of the cabbage data (n = 47 entries), most publications (83%) distinguished between red and white cabbages (var. *rubra* and *alba* respectively). Red cabbages (n = 18 entries) had a 17.5% higher SMCSO content when compared to white cabbages (n = 21 entries) (median [IQR]: 114 [96–127] mg/100 g, and 97 [67 – 122] mg/100 g, respectively). However, of the total 11 publications exploring SMCSO in cabbages, one publication was responsible for the entire available data

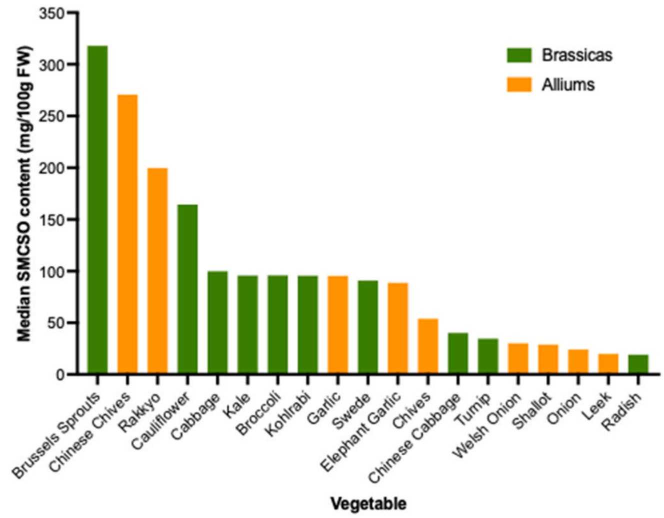

Fig. 2. Median SMCSO content (mg/100 g FW) of individual vegetables with ≥3 publications. FW, fresh weight; SMCSO, S-methyl cysteine sulfoxide.

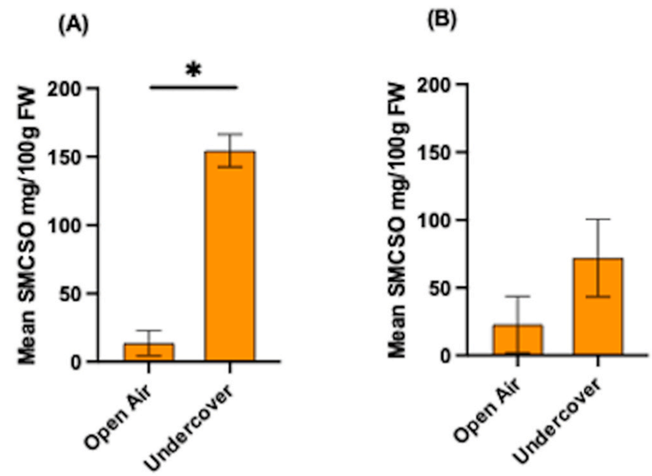

Fig. 3. The SMCSO content (mean ± standard error of the mean) of onions grown in open air (n = 33) versus undercover (n = 52), shown as (A) unadjusted and (B) adjusted for publication identification. Undercover-grown onions included a combination of greenhouse-grown (n = 48), both greenhouse and field-grown periods (n = 2) and hydroponically grown (n = 2). * indicates a statistically significant difference ($p < 0.05$). FW, fresh weight; SMCSO S-methyl cysteine sulfoxide.

compiled on red cabbages, and for 77% of the total data entries for cabbage. Similarly, when reporting onions (n = 158), the majority (n = 150) were identified simply as "*Allium cepa*", median [IQR]: 24 [12−126]) mg/100 g FW, with few publications distinguishing brown onions (n = 3 entries from 2 publications; median [IQR]: 17 [6 – 27] mg/100 g FW) from red onions (n = 5 from 1 publication; median [IQR]: 27 [22 – 29] mg/100 g FW). With so few publications (i.e., ≤2) distinguishing the differences between brown and red onions, or red and white cabbages, the variation in SMCSO levels according to colour must be treated with caution. In line with our criteria (compiling SMCSO data reported in a vegetable given by ≤2 publications), we have excluded these colour variations (brown/white onions, and red cabbages) from Table 1. The SMCSO levels in white cabbages were reported by four publications and are therefore included separately in Table 1.

Lastly, elephant garlic (also known as giant garlic or broadleaf wild leek), was reported in four publications. One publication reported on the SMCSO content of leaves (97 mg/100 g FW; grown in the Czech Republic), another reported specifically on the clove (mean 91 mg/100 g from four samples; grown in Italy), whilst the remaining two reported the SMCSO content of the 'edible' portion (grown in Korea), and the clove (country of growth not reported) with levels of 45 and 85 mg/100 g FW, respectively.

3.3. Variables influencing SMCSO content in vegetables

The mean SMCSO levels in onions grown under open air (n = 33) were 141 mg/100 g FW lower than those grown undercover (n = 52); [mean (SEM): 13.6 (9.32) and 154.49 (11.92) mg/100 g FW, respectively] (Fig. 3**A**). This difference was reduced to 49 mg/100 g and lost significance after adjusting for publication ID [mean (SEM): 22.81 (20.99) and 72.03 (28.74), respectively] (Fig. 3**B**).

A number of publications did not report the year that their samples were harvested. For those that did, we explored whether the levels of SMCSO changed in vegetables over time. We found that increasing time (i.e., increasing the year of reported harvest sampling), was a significant predictor of higher SMCSO content (mg/100 g FW) for garlic [coefficient (95% CI)]: 2.33 (1.27, 3.40), whilst both onion [-6.39 (-7.64, −5.13)] and kale [-4.92 (-6.15, −3.69)], were more likely to be lower. After adjusting for publication ID, we noted that with time (i.e., each progressive year of harvest sampling), the level of SMCSO (mg/100 g FW) was higher for garlic: [coefficient (95% CI)] 5.14 (0.00, 10.28), and remained lower for both onion [-2.70 (-5.58, 0.18)] and kale [-4.92 (-6.15, −3.69)], although only kale was statistically significant. We then explored the year of sampling as categorical. Noting the uneven heterogeneity of sample sizes across years of sampling, interpretation was difficult. Nonetheless, kale demonstrated a small, but significant reduction of SMCSO in the last three years of sampling (1981, 1985, and 1986) compared to baseline levels in 1974 (Fig. 4**)**.

Of the garlic entries (n = 175), almost all were grown in the northern hemisphere, with nearly 50% sourced from retail markets or directly from the producer or cultivator. Despite China being a major garlic producer (Liu et al., 2020), the SMCSO content of Chinese grown garlic was reported by only six publications (11 entries, sample size of 261). The garlics sampled in 2018 (Fig. 4C) reported a mean SMCSO of 532 mg/100 g FW averaged from 242 samples grown across six provinces in China (i.e., only one entry reported by one publication). This value is considerably higher than all of the other garlic entries grown in China (n = 10) which collectively had a mean 114 mg/100 g FW (median [IQR] 124 [82 – 133] mg/100 g FW) of SMCSO. In comparison, the mean SMCSO for all garlic entries grown outside of China (13 publications, 164 entries, sample size of 857) was 104 mg/100 g (median [IQR] 92 [55 – 146] mg/100 g FW). Over half of all the compiled garlics were grown in an open field with the remainder not reported. Five publications reported changes to SMCSO (and other sulfur-containing compounds) during various times of post-harvest storage (n = 3 publications for garlic and n = 2 for onion). The storage times for garlic ranged from 0 to 10 months post-harvest under temperature ranges of 0 °C to 20 °C, whilst storage times for onion ranged from 0 to 6 months. After adjusting for publication ID, we noted that SMCSO levels were lower for both garlic and onion as storage time increased [coefficient, (95% CI)] garlic: −0.46, (-1.76, 0.84); onion: −0.92, (-2.20, 0.35). Furthermore, higher storage temperature of garlic was associated with a marginal, albeit non-significant, higher SMCSO level [publication ID-adjusted coefficient (95% CI)] 0.67 (-1.51, 2.84).

The SMCSO content of kale was found to be significantly higher when harvested in winter; following adjustment for publication ID, [winter mean (SEM): 105.88 (6.59), in comparison to autumn: 81.66 (7.17) and summer: 53.06 (13.17) mg/100 g], as shown in Fig. 5.

3.4. Cooked and/or processed vegetables

Ten publications (Supplementary Table 10) quantified SMCSO content across six vegetables (broccoli, cabbage, hooker chives, garlic,

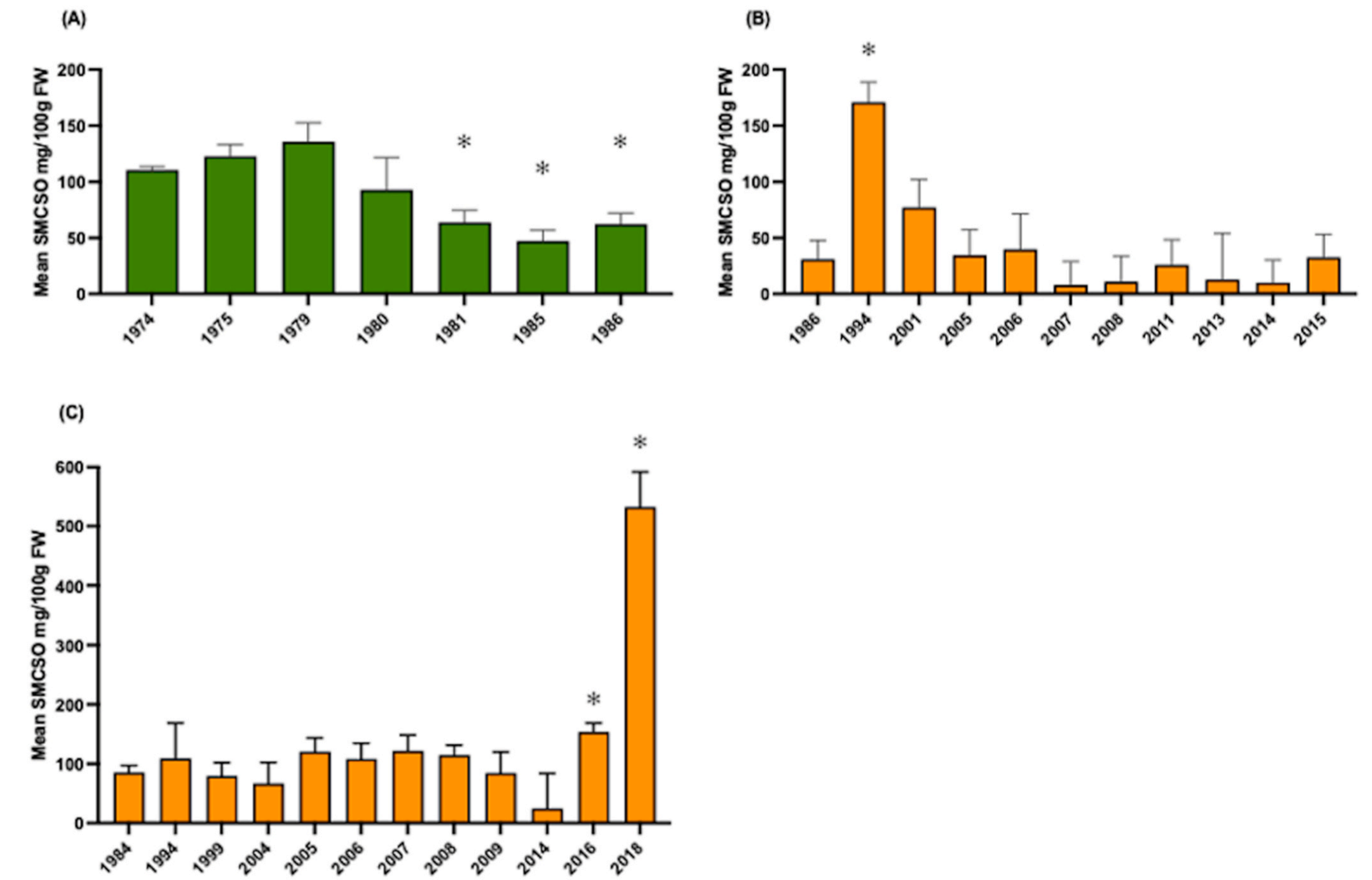

Fig. 4. The mean SMCSO content (mg/100 g FW), reported over time, graphed as mean (and standard error of the mean) for (**A**) kale, (**B**) onion, and (**C**) garlic, using mixed methods modelling adjusted for publication ID as a random factor, and year of sampling entered as categorical. Number of entries per year are (**A**) 1974 (n = 84), 1975 (n = 8), 1979 (n = 3), 1980 (n = 1), 1981 (n = 8), 1985 (n = 10), 1986 (n = 10); (**B**) 1986 (n = 5), 1994 (n = 45), 2001 (n = 4), 2005 (n = 6), 2006 (n = 2), 2007 (n = 9), 2008 (n = 6), 2011 (n = 6), 2013 (n = 1), 2014 (n = 11), 2015 (n = 10); and for (**C**) 1984 (n = 24), 1994 (n = 1), 1999 (n = 9), 2004 (n = 3), 2005 (n = 9), 2006 (n = 6), 2007 (n = 7), 2008 (n = 25), 2009 (n = 3), 2014 (n = 1), 2016 (n = 41), 2018 (n = 1). * indicates a statistically significant difference ($p < 0.05$) in SMCSO (mg/100 g) levels between the year of sampling compared to the earliest year of sampling. i.e., compared to 1974 (A), 1986 (B), or 1984 (C). FW, fresh weight; SMCSO, S-methyl cysteine sulfoxide.

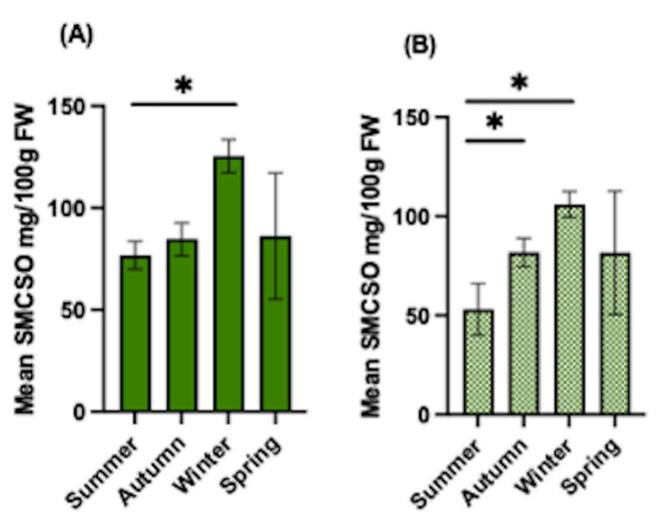

Fig. 5. The SMCSO mean and standard error of the mean comparing kale measurements across harvest seasons, shown as both (A) unadjusted and (B) adjusted for publication identification. Summer (n = 20), autumn (n = 53), winter (n = 50), and spring (n = 1). Kales with unknown harvest season (n = 3) were excluded from this analysis. * indicates a statistically significant difference between harvest seasons ($p < 0.05$). FW fresh weight; SMCSO, S-methyl cysteine sulfoxide.

onion, and radish) with each differing in their cooking and processing methods. As these did not meet our criteria (i.e., reported by ≤2 publications), these are provided in Supplementary Table 8 and comparisons were not possible.

3.5. *Animal forage*

Rape is a common forage used for livestock. We found four publications (69 entries) measuring SMCSO content in whole rape (i.e., leaves, petiole, stem, or whole plant) giving a total sample size of 392, sourced from either a trial (n = 38) or a Department, Association or Research Institute (n = 31). The median [IQR] for rape was 364 [12 – 538] mg/100 g DW, with almost all being grown in an open field (80%). The median [IQR] of SMCSO for rape harvested during summer was 332 [297 – 511], autumn 416 [353 – 495], winter 15 [8 – 607], and spring 12 [10–15] mg/100 g DW, with spring harvests reporting significantly lower SMCSO levels than both summer ($p = 0.0485$) and autumn ($p = 0.0128$) harvests.

3.6. *Analytical methods*

Various analytical methods were used in the measurements compiled for this database. Almost 57% of the total number of entries analysed SMCSO using high-performance liquid chromatography (HPLC) [n = entries (sample size)] [n = 391 (2384)], with the remaining methods being gas chromatography [n = 32 (53)], capillary electrophoresis [n = 23 (37)], ion exchange chromatography [n = 52 (112)], electrophoresis [n = 62 (180)], column chromatography [n = 54 (162)], thin layer chromatography [n = 7 (7)], amino acid analysis [n = 64 (118)], nuclear magnetic resonance spectroscopy [n = 2 (2)], or not reported [n = 3 (3)]. We also explored whether SMCSO levels for each available vegetable were different according to the analytical method used. For this, we differentiated the SMCSO levels measured by HPLC (the most common methodology) compared to all other analytical methods combined (i.e., as listed above). Overall, HPLC measured higher SMCSO levels in five vegetables (chives, garlic, onion, Welsh onion, and kale) with a median difference ranging between 2 and 133 mg/100 g FW, whilst the remaining 14 vegetables reported lower levels via HPLC (between 5 and 73 mg/100 g FW) (Supplementary Table 11). The difference in reported SMCSO levels between those measured via HPLC versus all other methods combined was not statistically significant. However, the exception was shallot which measured 11 mg/100 g FW lower in SMCSO content when measured via HPLC ($p = 0.0145$).

4. Discussion

We have compiled SMCSO data from commonly consumed vegetables into a food composition database. Data was limited to ten brassica and nine allium vegetables, with the first known record dating back to 1956.

Of the 705 data entries included in our main analysis (i.e., Table 1), ~25% were measured in vegetables intended for feeding livestock. These entries were included as they were deemed accessible for human consumption (i.e., cabbage, cauliflower, kale, onion, radish, swede, and turnip). Whilst we would have ideally preferred to limit our search to vegetables for commercial use only, this would have further limited the data available.

We identified a scarcity of research measuring SMCSO in commonly consumed vegetables. For example, the SMCSO content of broccoli was measured and reported in just nine publications, and cauliflower in eight publications, despite both being common vegetables for human consumption. Furthermore, despite being a well-known brassica consumed by humans, Brussels sprouts was quantified and reported in only three publications, although contained the highest level of SMCSO. Meanwhile, of our aggregated data on cabbage, 77% were only recently published (Friedrich et al., 2022) contributing 93% of our total pooled sample size for cabbages.

Our results suggest the level of SMCSO in brassica vegetables has changed over time. Previously, it was reported that SMCSO in Brussels sprouts ranged from 70 mg/100 g FW (Marks et al., 1992) to 167 mg/100 g FW (Smith, 1978). Our compiled data on Brussels sprouts report SMCSO to be considerably higher at 318 mg/100 g FW. Of the available entries for Brussels sprouts (n = 3), all were from a commercial retail source, although only one reported the year of sampling (i.e., 1999). The earliest measurement of SMCSO reported in Brussels sprouts was published in 1992 (mean 68 mg/100 g, measured via HPLC) (Marks et al., 1992), the second was in 2001 (mean 318 mg/100 g, measured via GC) (Kubec et al., 2001) and the third measurement in 2019 (mean 420 mg/100 g, via HPLC) (Coode-Bate et al., 2019). With so few measurements measuring SMCSO levels in Brussels sprouts, interpretation regarding either changes over time or analytical method is limited. Previously, Morris and Thompson (1956) reported a 150 g serving of equal parts of broccoli and cauliflower florets to contain ~360 mg of SMCSO (equivalent to 240 mg/100 g FW). Using our compiled SMCSO data we estimate this to be substantially lower at ~130.5 mg/100 g FW. The overall level of SMCSO within kale has reduced over time, although this is likely due to purposeful reductions by the cattle and agricultural industry to prevent kale anaemia factor and related changes in ruminants (Edmands et al., 2013).

We did not report on vegetables grown under manipulated experimental conditions (e.g., variations in sulfur application) as they were not likely to be commercially available for human consumption. It is known that raising the amount of sulfur available during growth (via fertilisers) results in higher SMCSO accumulation in both garlic and onions (Kopsell et al., 2007; Kopsell et al., 2003; Randle et al., 1995; Resemann & Carle, 2003). This is due to SMCSO being considered a reliable sulfur sink (i.e., readily stores available sulfur), especially in the early growth and developmental stages of allium bulbs (Randle et al., 2002; Randle et al., 1995). Furthermore, it is recognised that plant genetics, cultivar, maturity, growing conditions, as well as the section of the plant being measured, all influence the levels of sulfur-containing compounds (such as SMCSO) reported (Hornickova et al., 2010; Nguyen et al., 2020; Petropoulos et al., 2017b; Wu et al., 2021). For example, a kale plant can decrease 5-fold in SMCSO as it transitions from young to old leaves (Gosden, 1979), whilst levels have been shown to be lower in radish leaves compared to radish bulbs (Stewart & Judson, 2004). Variability in geographical location, cultivar and ecotype were acknowledged by Liu et al. (2020) as likely behind the considerable SMCSO range (between 26 and 1284 mg/100 g FW) reported in garlics grown and sampled across six provinces in China. As more research becomes available, these factors influencing SMCSO variability can be explored in more detail.

Lastly, despite knowing that research has heavily favoured other sulfur-based compounds such as GSLs, it was still somewhat surprising to not have more publications reporting on changes to SMCSO content after cooking. Ko and Nile (2021) reported stir-frying as the best way to retain SMCSO in onions, followed by boiling, whilst steaming onions substantially reduced levels. As promising evidence on the potential role of SMCSO for human health continues to emerge, we anticipate an expansion of new research quantifying SMCSO levels in foods following exposure to various cooking methods.

4.1. Limitations

We have reported on SMCSO levels measured found within, and almost exclusively in brassicas and alliums. There are suggestions that a non-sulfoxide form (i.e., S-methyl cysteine) and/or a form bound to γ-glutamyl peptides, have been identified (although not quantified) in other plant-based foods (i.e., *Astragalus* and *Phaseolus* genera of the *Fabaceae* family (e.g., legumes) (Dunnill, 1967; Edmands et al., 2013; Giada, 1998). To support this, a recent dietary intervention revealed a >2-fold increase in SMCSO within the plasma metabolome of children consuming navy beans *(Phaseolus vulgaris)*, in comparison to those children that did not (Li et al., 2018). Until we have conclusive evidence for the presence of, and the concentration of SMCSO within a more varied array of foods, this remains a limitation to the comprehensiveness of this database.

The levels of sulfur-containing compounds within plants are influenced by various growing and environmental factors, such as the availability and uptake of sulfur and other nutrients, the application of different fertilizers, plant defence requirements, plant genetics, cultivar type, stages of growth, water supply, soil condition, atmosphere, as well as geographical location, time of harvest, storage, and handling conditions (Hill et al., 2022; Nguyen et al., 2020; Petropoulos et al., 2017b; Ramirez et al., 2017; Wu et al., 2021). It is likely that the level of SMCSO in plants are also similarly impacted by these factors. Whilst we noted that open-air-grown onions had lower SMCSO levels than those grown undercover, the latter were likely subjected to stricter control of growing conditions (i.e., set application of water, temperature, fertilizer, etc), which may well have positively impacted their growth, and subsequent SMCSO level. We were unable to confirm this due to a combination of inadequate and/or heterogenic data, and lack of reported detail across studies (e.g., many publications did not report on temperature, rainfall, nor type/s of fertilizer, whether sulfur-containing, and if so, at what level). In addition, there can be large heterogeneity in analytical methods employed to assess sulfur-containing compounds, with the 'same' method able to vary widely in terms of instrumentation and procedure, resulting in substantial differences in reported SMCSO levels (Ramirez et al., 2017; Wu et al., 2021). Further research into how each of these factors influence SMCSO levels in plant-based foods is needed so more detailed analysis and understanding is possible.

5. Conclusions

Brassica and allium vegetables likely contribute to the highest proportion of SMCSO intake in humans. This database has been compiled using SMCSO values reported from pre-existing scientific literature. It plays an important first step toward estimating dietary intakes of SMCSO in the population. During this process, we identified significant gaps, mainly around the scarcity of literature. This data shortage is evident in both the infrequency of SMCSO measurements in brassica and allium vegetables, as well as within other plant-based sources. To address the limitations discussed above, additional research is needed to quantify SMCSO in a wide variety of foods so this database can be expanded. This will enable more reliable estimation of SMCSO intakes. Furthermore, more detailed reporting is needed to enhance our understanding of factors (i.e., growth and environmental, cooking and processing methods) that impact the variability of SMCSO content within a wide range of foods available for human consumption.

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CRediT authorship contribution statement

Caroline R. Hill: Data curation, Formal analysis, Methodology, Writing – original draft, Investigation. **Emma L. Connolly:** Investigation, Writing – review & editing. **Armaghan Shafaei:** Supervision, Writing – review & editing. **Lois Balmer:** Supervision, Writing – review & editing. **Liezhou Zhong:** Writing – review & editing. **Taulant Muka:** Writing – review & editing. **Antonietta Hayhoe:** Writing – review & editing. **Shikha Saha:** Writing – review & editing. **Richard J. Woodman:** Formal analysis, Writing – review & editing. **Joshua R. Lewis:** Supervision, Writing – review & editing. **Jonathan M. Hodgson:** Supervision, Writing – review & editing. **Lauren C. Blekkenhorst:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

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Data Availability

Data will be made available on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jfca.2024.106151.

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