

APPENDIX 1 – EMBASE PRELIMINARY SEARCH STRATEGY

Embase (Embase.com) – 7253 references retrieved on 06 October 2020

One-line search run in Results tab of Embase.com platform:

('antioxidant'/exp OR antioxidant*:ti,ab,kw OR 'anti-oxidant*':ti,ab,kw OR antioxidat*:ti,ab,kw OR 'anti-oxidat*':ti,ab,kw OR 'antioxidant activity'/exp OR 'acetylcysteine'/exp OR acetylcystein*:ti,ab,kw OR 'acetyl cysteine':ti,ab,kw OR acetadote:ti,ab,kw OR mucomyst:ti,ab,kw OR cetylev:ti,ab,kw OR 'arginine'/exp OR arginin*:ti,ab,kw OR 'ascorbic acid'/exp OR 'ascorbic acid*':ti,ab,kw OR 'vitamin c':ti,ab,kw OR ascorbate:ti,ab,kw OR 'ascorbyl palmitate':ti,ab,kw OR 'carotenoid'/exp OR caroten*:ti,ab,kw OR 'coumarin'/exp OR coumarin*:ti,ab,kw OR cumarin*:ti,ab,kw OR 'curcumin'/exp OR curcumin*:ti,ab,kw OR turmeric:ti,ab,kw OR 'ellagic acid'/exp OR 'ellagic acid*':ti,ab,kw OR 'benzoanic acid*':ti,ab,kw OR 'benzoaric acid*':ti,ab,kw OR 'melatonin'/exp OR melatonin*:ti,ab,kw OR circadin:ti,ab,kw OR 'polyphenol'/exp OR polyphenol*:ti,ab,kw OR 'retinol'/exp OR retinol:ti,ab,kw OR 'vitamin a':ti,ab,kw OR 'retinyl palmitate':ti,ab,kw OR 'retinoic acid*':ti,ab,kw OR 'selenium'/exp OR selenium:ti,ab,kw OR selenicum:ti,ab,kw OR 'tocopherol'/exp OR tocopherol*:ti,ab,kw OR tocoferol:ti,ab,kw OR 'vitamin e':ti,ab,kw OR 'ubiquinone'/exp OR ubiquinone:ti,ab,kw OR 'vitamin q':ti,ab,kw OR 'coenzyme q10':ti,ab,kw OR coq10:ti,ab,kw OR 'coenzyme q':ti,ab,kw OR 'zinc'/exp OR zinc:ti,ab,kw OR zincum:ti,ab,kw OR 'thioctic acid'/exp OR 'thioctic acid*':ti,ab,kw OR 'lipoic acid*':ti,ab,kw OR 'resveratrol'/exp OR resveratrol:ti,ab,kw OR 'glutathione'/exp OR glutathione:ti,ab,kw OR glutathiol:ti,ab,kw OR 'chlorogenic acid'/exp OR 'chlorogenic acid*':ti,ab,kw OR 'ferulic acid'/exp OR 'ferulic acid*':ti,ab,kw OR 'ferulate sodium':ti,ab,kw OR 'sodium ferulate':ti,ab,kw OR 'lycopene'/exp OR lycopene:ti,ab,kw OR

'docosahexaenoic acid'/exp OR docosahexaeno*:ti,ab,kw OR 'icosapentaenoic acid'/exp OR 'icosapentaenoic acid*':ti,ab,kw OR 'eicosapentaenoic acid*':ti,ab,kw OR 'vitamin supplementation'/exp OR 'vitamin supplement*':ti,ab,kw OR 'hibiscus'/exp OR hibiscus:ti,ab,kw OR 'folic acid'/exp OR 'folic acid*':ti,ab,kw OR folate:ti,ab,kw OR 'catechin'/exp OR catechin*:ti,ab,kw OR 'catechuic acid*':ti,ab,kw OR ciandiol:ti,ab,kw OR 'anthocyanidin'/exp OR anthocyanidin:ti,ab,kw OR 'tannin'/exp OR tannin*:ti,ab,kw OR 'tannic acid*':ti,ab,kw OR gallotanni*:ti,ab,kw OR 'rutoside'/exp OR rutoside:ti,ab,kw OR rutin:ti,ab,kw OR rutin:ti,ab,kw OR 'vitamin p':ti,ab,kw OR 'isoflavone'/exp OR isoflavone*:ti,ab,kw OR 'quercetin'/exp OR quercetin*:ti,ab,kw OR quercitin*:ti,ab,kw OR quercetol*:ti,ab,kw OR 'lignan'/exp OR lignan*:ti,ab,kw OR 'allicin'/exp OR allicin:ti,ab,kw OR '5-methoxytryptamine'/exp OR methoxytryptamine:ti,ab,kw OR mexamine:ti,ab,kw OR 'uric acid'/exp OR 'uric acid*':ti,ab,kw OR 'urobilinogen'/exp OR urobilinogen:ti,ab,kw OR urinobilinogen:ti,ab,kw OR 'melanoidin'/exp OR melanoidin:ti,ab,kw OR 'phytic acid'/exp OR 'phytic acid*':ti,ab,kw OR 'phytinic acid*':ti,ab,kw OR 'saponin'/exp OR saponin*:ti,ab,kw OR glycosaponin*:ti,ab,kw OR 'methionine'/exp OR methionin*:ti,ab,kw OR levomethionine:ti,ab,kw OR methiolate:ti,ab,kw OR 'albumin'/exp OR albumin:ti,ab,kw OR albumen:ti,ab,kw OR 'lactoferrin'/exp OR lactoferrin*:ti,ab,kw OR lactotransferrin*:ti,ab,kw OR 'chromium'/exp OR chromium:ti,ab,kw OR 'transferrin'/exp OR transferrin*:ti,ab,kw OR siderophilin:ti,ab,kw OR 'ferritin'/exp OR ferritin*:ti,ab,kw OR immunoferritin:ti,ab,kw OR 'manganese'/exp OR manganese:ti,ab,kw OR cutaval:ti,ab,kw OR 'molybdenum'/exp OR molybden*:ti,ab,kw OR 'fish oil'/exp OR 'fish oil*':ti,ab,kw OR promega:ti,ab,kw OR 'omega 3 fatty acid'/exp OR 'omega 3 fatty acid*':ti,ab,kw OR 'omega 3 carboxylic acid*':ti,ab,kw OR 'alternative medicine'/de OR 'alternative medicine*':ti,ab,kw OR 'complementary

medicine*:ti,ab,kw OR 'complementary therap*:ti,ab,kw OR 'diet supplementation'/exp OR 'diet* supplement*:ti,ab,kw) AND ('chemotherapy'/exp OR chemotherap*:ti,ab,kw OR 'radiotherapy'/exp OR radiotherap*:ti,ab,kw OR 'cancer therapy'/exp OR (((cancer OR radiation OR irradiation OR tumor* OR tumour* OR neoplas* OR oncolog*) NEAR/3 (therap* OR treat* OR inhibit*)):ti,ab,kw) OR 'adjuvant radiotherapy'/exp OR 'antineoplastic agent'/exp OR anticancer*:ti,ab,kw OR 'anti-cancer*:ti,ab,kw OR anticarcinogen*:ti,ab,kw OR 'anti-carcinogen*:ti,ab,kw OR 'antineoplastic activity'/exp OR antineoplastic*:ti,ab,kw OR 'anti-neoplastic*:ti,ab,kw OR antitumor:ti,ab,kw OR 'anti-tumor':ti,ab,kw OR antitumour:ti,ab,kw OR 'anti-tumour':ti,ab,kw OR 'chemoradiotherapy'/exp OR chemoradiotherap*:ti,ab,kw OR 'alkylating agent*:ti,ab,kw OR alkylator*:ti,ab,kw OR 'antimetabolite'/exp OR antimetaboli*:ti,ab,kw OR 'anti-metaboli*':ti,ab,kw OR 'antimitotic agent'/exp OR antimitotic*:ti,ab,kw OR 'anti-mitotic*:ti,ab,kw OR 'mitotic inhibitor*:ti,ab,kw OR 'mitosis inhibitor*:ti,ab,kw OR 'anthracycline'/exp OR anthracyclin*:ti,ab,kw OR 'protein tyrosine kinase inhibitor'/exp OR 'tyrosine kinase inhibitor*:ti,ab,kw OR tki:ti,ab,kw OR 'tyrosine protein kinase inhibitor*:ti,ab,kw OR 'protein serine threonine kinase inhibitor'/exp OR 'serine threonine kinase inhibitor*:ti,ab,kw OR 'checkpoint inhibitor'/exp OR 'checkpoint inhibitor*:ti,ab,kw OR 'anti pd1':ti,ab,kw OR 'anti pdl1':ti,ab,kw OR 'antimyeloma activity'/exp OR antimyeloma*:ti,ab,kw OR 'anti-myeloma*:ti,ab,kw OR 'dna topoisomerase inhibitor'/exp OR 'topoisomerase inhibitor*:ti,ab,kw OR 'topoisomerase 1 inhibitor*:ti,ab,kw OR 'topoisomerase i inhibitor*:ti,ab,kw OR 'antiandrogen'/exp OR 'antiandrogen therapy'/exp OR 'anti-androgen*:ti,ab,kw OR antiandrogen*:ti,ab,kw OR 'androgen antagonist*:ti,ab,kw OR 'antiestrogen'/exp OR 'anti-estrogen*:ti,ab,kw OR 'anti-oestrogen*:ti,ab,kw OR antiestrogen*:ti,ab,kw OR antioestrogen*:ti,ab,kw OR 'estrogen antagonist*:ti,ab,kw OR

'oestrogen antagonist':ti,ab,kw OR 'cancer hormone therapy'/exp OR 'cancer hormone therap*':ti,ab,kw OR 'cancer patient'/exp OR 'cancer patient*':ti,ab,kw OR 'oncolog* patient*':ti,ab,kw OR electrochemotherap*':ti,ab,kw OR photochemotherap*':ti,ab,kw OR chemoembolization:ti,ab,kw OR chemoembolisation:ti,ab,kw OR carcinochemotherap*':ti,ab,kw OR multichemotherap*':ti,ab,kw OR polychemotherap*':ti,ab,kw OR antileukemi*':ti,ab,kw OR 'anti-leukemi*':ti,ab,kw OR antileukaemi*':ti,ab,kw OR 'anti-leukaemi*':ti,ab,kw OR antimetasta*':ti,ab,kw OR 'anti-metasta*':ti,ab,kw OR antimutagen*':ti,ab,kw OR 'anti-mutagen*':ti,ab,kw) AND (metaanaly*':ti,ab,kw OR 'met analy*':ti,ab,kw OR 'meta analy*':ti,ab,kw OR metanaly*':ti,ab,kw OR 'meta analysis'/exp OR 'meta analysis (topic)'/exp OR 'systematic review'/exp OR 'systematic review (topic)'/exp OR (((systematic* OR methodologic* OR collaborative OR integrative) NEAR/3 (review* OR overview*)):ti,ab,kw OR ((pool* NEAR/3 analy*):ti,ab,kw) OR handsearch*':ti,ab,kw OR 'hand search*':ti,ab,kw OR 'data synthes*':ti,ab,kw OR 'data extraction*':ti,ab,kw OR 'data abstraction*':ti,ab,kw OR metaregression*':ti,ab,kw OR 'meta regression*':ti,ab,kw OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

APPENDIX 2 – DRAFT ELEMENTS FOR DATA CHARTING**Bibliographic characteristics**

Journal name
Year of publication
Country of corresponding author
Funding

Review question and methods

Review protocol cited/provided
Inclusion criteria for participants: types of cancer(s), stage, other disease characteristics
Inclusion criteria for participants: age, sex, other demographic characteristics
Inclusion criteria for participants: cancer treatment(s)
Inclusion criteria for interventions: specific supplements or categories of supplements
Inclusion criteria for comparators:
Outcomes sought from included studies (including not only domain but also instrument or scale and time frame if specified): [may break down by type eg, quality of life, adverse effect, success of cancer treatment]
Study designs eligible for inclusion:
List of databases searched
Total number of databases searched
Date of last database search
Quality assessment tool
Planned meta-analyses, subgroup analyses and sensitivity analyses

Planned methods to assess the quality/certainty of effect estimate
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Review results and analyses from included* RCTs

Number of included RCTs
Number of participants in included RCTs
Age, sex, other demographic characteristics of participants in included RCTs
Cancer characteristics of participants in included RCTs
Cancer treatment(s) provided to participants in included RCTs
Antioxidant interventions in included RCTs
Comparators in included RCTs:
Outcomes present in included RCTs:
List of meta-analyses conducted
List of subgroup analyses conducted
List of sensitivity analyses conducted

*all references to included studies refer to those studies assessing effects of oral antioxidant supplement interventions during curative treatment for cancer; systematic reviews may have a broader scope.

For each review, results for each antioxidant-related PICO question

Participant/Intervention/Comparator/Outcome/Time (may group multiple time points)
Are any results presented?
If so, were results qualitative or quantitative?
If quantitative, what was the effect estimate?
Quote or summary of author assessment of findings on the PICO question

Certainty/quality of evidence for the results (if assessed by authors)
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Confidence in results of the review (see AMSTAR 2 assessment)

APPENDIX 3 – AMSTAR-2 CRITERIA FOR CONFIDENCE IN THE RESULTS OF SYSTEMATIC REVIEWS

AMSTAR-2 criteria [47]
1. Did the research questions and inclusion criteria for the review include the components of PICO? (Y, N)
2. Did the report of the review contain explicit statement that the review methods were established prior to conduct of the review? (Y, PY, N)
3. Did the review authors explain their selection of the study designs for inclusion in the review? (Y, N)
4. Did the reviewer authors use a comprehensive literature search strategy? (Y, PY, N) CRITICAL FLAW if not Y, PY
5. Did the review authors perform study selection in duplicate? (Y, N)
6. Did the review authors perform data extraction in duplicate? (Y, N)
7. Did the review authors provide a list of excluded studies and justify the exclusions? (Y, PY, N)
8. Did the review authors describe the included studies in adequate detail? (Y, PY, N)
9A. RCTS- Did authors use a satisfactory technique for assessing the risk of bias (ROB) in individual studies that were included in the review? (Y, PY, N, NA- includes only NRSI) CRITICAL FLAW if not Y, PY
9B. NRSI- Did authors use a satisfactory technique for assessing the risk of bias (ROB) in individual studies that were included in the review? (Y, PY, N, NA- includes only RCTs) CRITICAL FLAW if not Y, PY

10. Did the review authors report on the sources of funding for the included studies? (Y, N)
11A. RCTs- If meta-analysis was performed did the authors use appropriate methods for statistical combination of results? (Y,N, only NRSI, No MA) CRITICAL FLAW if not Y, PY
11B. NRSI- If meta-analysis was performed did the authors use appropriate methods for statistical combination of results? (Y,N, only RCTs, no MA) CRITICAL FLAW if not Y, PY
12. If meta-analysis was performed, did the review authors assess the potential impact of ROB in individual studies on the results of the meta-analysis or other evidence synthesis? (Y, N, No MA, No QA)
13. Did the review authors account for ROB in individual studies when interpreting/discussing the results of the review? (Y, N, No QA) CRITICAL FLAW if not Y, PY
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? (Y, N)
15. Did the review authors carry out an adequate investigation of publication bias, and discuss its likely impact on the results of the review? (Y, N)
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for the review? (Y, N)
Number of critical flaws (critical items answered N):
Number of non-critical flaws (non-critical items answered N):
Rubric for overall confidence: High confidence: no critical flaws with zero or one non-critical flaw.

Moderate confidence: no critical flaws with > 1 non-critical flaw. Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence

Low confidence: one critical flaw with or without any non-critical flaws

Critically low confidence: more than one 1 critical flaw with or without any non-critical flaws.

Overall confidence in the results of the review (High/Moderate/Low/Critically Low):

Interpretation of quality levels:

High: The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

Moderate: The systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review

Low: The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest

Critically Low: The review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies