**Appendix A.** Search strategy

A systematic review and meta-analysis of the CoQ10 eﬀects on oxidative stress

|  |  |
| --- | --- |
| **Groups** | **Descriptors** |
| Outcome | Glutathione Reductase OR Reductase, Glutathione OR Glutathione Peroxidase OR Peroxidase Glutathione OR Superoxide Dismutase OR Dismutase Superoxide OR Oxidative Stress OR Stress Oxidative OR Stress, Oxidative OR Total Antioxidant Capacity OR Total Antioxidant Status OR antioxidant OR Oxidant OR reactive oxygen species OR Catalase OR Oxygen Radical Absorbance OR reactive nitrogen species OR protein carbonyl OR lipid peroxide OR Total Radical Trapping Antioxidant Parameter OR Malondialdehyde OR Nitric oxide OR 8-hydroxydeoxyguanosine OR thiobarbituric acid reactive substances OR nitrotyrosine OR sulfhydryl group OR oxidized LDL lipoprotein OR xanthine oxidase OR paraoxonase-1 |
| Exposure | Coenzyme Q10 OR Co-enzyme Q10 OR Coenzyme Q OR “Q10” OR CoQ10 OR Ubiquinone OR Ubiquinone 10 OR 2,3-dimethoxy-5-methyl-6-decaprenylbenzoquinone OR Ubidecarenone OR Ubiquinone 50 OR Bio-Quinone Q10 OR Ubisemiquinone radical OR Q-ter OR Ubisemiquinone OR Ubiquinol-10 OR Ubiquinol |
| Setting | Randomized controlled trial OR controlled clinical trial OR randomized controlled trials OR random allocation OR double blind method OR single blind method OR clinical trial OR clinical trials OR placebos OR placebo OR random |

**PUBMED**

**Number of localized studies:** 539

**Limits:** humans

**Number of studies after applying limits:** 450

|  |  |  |
| --- | --- | --- |
|  | **Descriptors** | Number of studies reached |
| **#1** | ((((((((((((((((((((((((((((((("Glutathione Reductase"[Mesh] OR ("glutathione reductase"[MeSH Terms] OR ("glutathione"[All Fields] AND "reductase"[All Fields]) OR "glutathione reductase"[All Fields] OR ("reductase"[All Fields] AND "glutathione"[All Fields]) OR "reductase, glutathione"[All Fields])) OR "Glutathione Peroxidase"[Mesh]) OR (("peroxidases"[MeSH Terms] OR "peroxidases"[All Fields] OR "peroxidase"[All Fields] OR "peroxidase"[MeSH Terms]) AND ("glutathione"[MeSH Terms] OR "glutathione"[All Fields]))) OR ("superoxide dismutase"[MeSH Terms] OR ("superoxide"[All Fields] AND "dismutase"[All Fields]) OR "superoxide dismutase"[All Fields])) OR "Superoxide Dismutase"[Mesh]) OR (Dismutase[All Fields] AND ("superoxides"[MeSH Terms] OR "superoxides"[All Fields] OR "superoxide"[All Fields]))) OR "Oxidative Stress"[Mesh]) OR ("oxidative stress"[MeSH Terms] OR ("oxidative"[All Fields] AND "stress"[All Fields]) OR "oxidative stress"[All Fields] OR ("stress"[All Fields] AND "oxidative"[All Fields]) OR "stress oxidative"[All Fields])) OR ("oxidative stress"[MeSH Terms] OR ("oxidative"[All Fields] AND "stress"[All Fields]) OR "oxidative stress"[All Fields] OR ("stress"[All Fields] AND "oxidative"[All Fields]) OR "stress, oxidative"[All Fields])) OR (Total[All Fields] AND ("antioxidants"[Pharmacological Action] OR "antioxidants"[MeSH Terms] OR "antioxidants"[All Fields] OR "antioxidant"[All Fields]) AND Capacity[All Fields])) OR "Antioxidants"[Mesh]) OR "Oxidants"[Mesh]) OR "Reactive Oxygen Species"[Mesh]) OR "Catalase"[Mesh]) OR "Oxygen Radical Absorbance Capacity"[Mesh]) OR "Reactive Nitrogen Species"[Mesh]) OR (("proteins"[MeSH Terms] OR "proteins"[All Fields] OR "protein"[All Fields]) AND carbonyl[All Fields])) OR "Lipid Peroxides"[Mesh]) OR (Total[All Fields] AND Radical[All Fields] AND Trapping[All Fields] AND ("antioxidants"[Pharmacological Action] OR "antioxidants"[MeSH Terms] OR "antioxidants"[All Fields] OR "antioxidant"[All Fields]) AND Parameter[All Fields])) OR "Malondialdehyde"[Mesh]) OR "Nitric Oxide"[Mesh]) OR "8-oxo-7-hydrodeoxyguanosine"[Supplementary Concept]) OR "Thiobarbituric Acid Reactive Substances"[Mesh]) OR "3-nitrotyrosine"[Supplementary Concept]) OR ("3-nitrotyrosine"[Supplementary Concept] OR "3-nitrotyrosine"[All Fields] OR "nitrotyrosine"[All Fields])) OR "Sulfhydryl Compounds"[Mesh]) OR ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR ("sulfhydryl"[All Fields] AND "group"[All Fields]) OR "sulfhydryl group"[All Fields])) OR "oxidized low density lipoprotein"[Supplementary Concept]) OR (("oxidized low density lipoprotein"[Supplementary Concept] OR "oxidized low density lipoprotein"[All Fields] OR "oxidized ldl"[All Fields]) AND ("lipoproteins"[MeSH Terms] OR "lipoproteins"[All Fields] OR "lipoprotein"[All Fields]))) OR "Xanthine Oxidase"[Mesh]) OR "Aryldialkylphosphatase"[Mesh]) OR ("aryldialkylphosphatase"[MeSH Terms] OR "aryldialkylphosphatase"[All Fields] OR "paraoxonase 1"[All Fields]) | 631616 |
| **#2** | ((((((((((((((("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "coenzyme q10"[All Fields]) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "co enzyme q10"[All Fields])) OR ("ubiquinone"[MeSH Terms] OR "ubiquinone"[All Fields] OR "coenzyme q"[All Fields])) OR Q10[All Fields]) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "coq10"[All Fields])) OR ("ubiquinone"[MeSH Terms] OR "ubiquinone"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "ubiquinone 10"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "ubidecarenone"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "ubiquinone 50"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "bio quinone q10"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "ubisemiquinone radical"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "q ter"[All Fields])) OR ("coenzyme Q10"[Supplementary Concept] OR "coenzyme Q10"[All Fields] OR "ubisemiquinone"[All Fields])) OR ("ubiquinol-10"[Supplementary Concept] OR "ubiquinol-10"[All Fields] OR "ubiquinol 10"[All Fields])) OR ("ubiquinol"[Supplementary Concept] OR "ubiquinol"[All Fields]) | 17233 |
| **#3** | ((((((((("Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type]) OR "Randomized Controlled Trials as Topic"[Mesh]) OR "Random Allocation"[Mesh]) OR "Double-Blind Method"[Mesh]) OR "Single-Blind Method"[Mesh]) OR "Clinical Trial"[Publication Type]) OR ("clinical trial"[Publication Type] OR "clinical trials as topic"[MeSH Terms] OR "clinical trials"[All Fields])) OR "Placebos"[Mesh]) OR ("placebos"[MeSH Terms] OR "placebos"[All Fields] OR "placebo"[All Fields])) OR ("random allocation"[MeSH Terms] OR ("random"[All Fields] AND "allocation"[All Fields]) OR "random allocation"[All Fields] OR "random"[All Fields]) | 1535248 |
| **#4** | **#1** AND **#2** AND #3 | 539 |

**WEB OF SCIENCE**

**Number of localized studies:** 497

**Limits:** documents types (articles)

**Number of studies after applying limits:** 339

|  |  |  |
| --- | --- | --- |
|  | **Descriptors** | Number of studies reached |
| **#1** | TS=(“Glutathione Reductase”) OR TS=(“Reductase, Glutathione”) OR TS=(“Glutathione Peroxidase”) OR TS=(“Peroxidase Glutathione”) OR TS=(Superoxide Dismutase) OR TS=(“Dismutase Superoxide”) OR TS=(“Oxidative Stress”) OR TS=(“Stress Oxidative”) OR TS=(“Stress, Oxidative”) OR TS=(“Total Antioxidant Capacity”) OR TS=(“Total Antioxidant Status”) OR TS=(“antioxidant”) OR TS=(“Oxidant”) OR TS=(“reactive oxygen species”) OR TS=(“Catalase”) OR TS=(“Oxygen Radical Absorbance”) OR TS=(“reactive nitrogen species”) OR TS=(“protein carbonyl”) OR TS=(“lipid peroxide”) OR TS=(“Total Radical Trapping Antioxidant Parameter”) OR TS=(“Malondialdehyde ”) OR TS=(“Nitric oxide”) OR TS=(“8-hydroxydeoxyguanosine”) OR TS=(“thiobarbituric acid reactive substances”) OR TS=(“nitrotyrosine”) OR TS=(“sulfhydryl group”) OR TS=(“oxidized LDL lipoprotein”) OR TS=(“xanthine oxidase”) OR TS=(“paraoxonase-1”) | 845984 |
| **#2** | TS=(“Coenzyme Q10”) OR TS=(“Co-enzyme Q10”) OR TS=(“Coenzyme Q”) OR TS=(“Q10”) OR TS=(“CoQ10”) OR TS=(“Ubiquinone”) OR TS=(“Ubiquinone 10”) OR TS=(“2,3-dimethoxy-5-methyl-6-decaprenylbenzoquinone”) OR TS=(“Ubidecarenone”) OR TS=(“Ubiquinone 50”) OR TS=(“Bio-Quinone Q10”) OR TS=(“Ubisemiquinone radical”) OR TS=(“Q-ter ”) OR TS=(“Ubisemiquinone”) OR TS=(“Ubiquinol-10”) OR TS=(“Ubiquinol ”) | 17014 |
| **#3** | TS=(Randomized controlled trial) OR TS=(controlled clinical trial) OR TS=(randomized controlled trials) OR TS=(random allocation) OR TS=(double blind method) OR TS=(single blind method) OR TS=(clinical trial) OR TS=(clinical trials) OR TS=(placebos) OR TS=(placebo) OR TS=(random) | 1593672 |
| **#4** | **#1** AND **#2** AND **#3** | 497 |

**SCOPUS**

**Number of localized studies:** 1591

**Limits:** *document type* (article and article in press)

**Number of studies after applying limits:** 751

|  |  |  |
| --- | --- | --- |
|  | **Descriptors** | Number of studies reached |
| **#1** | ( ( TITLE-ABS-KEY ( glutathione AND reductase ) ) OR ( TITLE-ABS-KEY ( reductase, AND glutathione ) ) OR ( TITLE-ABS-KEY ( glutathione AND peroxidase ) ) OR ( TITLE-ABS-KEY ( peroxidase AND glutathione ) ) OR ( TITLE-ABS-KEY ( superoxide AND dismutase ) ) ( TITLE-ABS-KEY ( dismutase AND superoxide ) ) OR ( TITLE-ABS-KEY ( oxidative AND stress ) ) OR ( TITLE-ABS-KEY ( stress AND oxidative ) ) OR ( TITLE-ABS-KEY ( stress, AND oxidative ) ) ) OR ( ( TITLE-ABS-KEY ( stress, AND oxidative ) ) OR ( TITLE-ABS-KEY ( total AND antioxidant AND capacity ) ) OR ( TITLE-ABS-KEY ( total AND antioxidant AND status ) ) OR ( TITLE-ABS-KEY ( antioxidant ) ) OR ( TITLE-ABS-KEY ( oxidant ) ) OR ( TITLE-ABS-KEY ( reactive AND oxygen AND species ) ) OR ( TITLE-ABS-KEY ( catalase ) ) ) OR ( ( TITLE-ABS-KEY ( oxygen AND radical AND absorbance ) ) OR ( TITLE-ABS-KEY ( reactive AND nitrogen AND species ) ) OR ( TITLE-ABS-KEY ( protein AND carbonyl ) ) OR ( TITLE-ABS-KEY ( lipid AND peroxide ) ) OR ( TITLE-ABS-KEY ( total AND radical AND trapping AND antioxidant AND parameter ) ) OR ( TITLE-ABS-KEY ( malondialdehyde ) ) OR ( TITLE-ABS-KEY ( nitric AND oxide ) ) ) OR ( ( TITLE-ABS-KEY ( 8-hydroxydeoxyguanosine ) ) OR ( TITLE-ABS-KEY ( thiobarbituric AND acid AND reactive AND substances ) ) OR ( TITLE-ABS-KEY ( nitrotyrosine ) ) OR ( TITLE-ABS-KEY ( sulfhydryl AND group ) ) OR ( TITLE-ABS-KEY ( oxidized AND ldl AND lipoprotein ) ) OR ( TITLE-ABS-KEY ( xanthine AND oxidase ) ) OR ( TITLE-ABS-KEY ( paraoxonase-1 ) ) ) | 969439 |
| **#2** | ( ( TITLE-ABS-KEY ( coenzyme AND q10 ) ) OR ( TITLE-ABS-KEY ( co-enzyme AND q10 ) ) OR ( TITLE-ABS-KEY ( q10 ) ) OR ( TITLE-ABS-KEY ( coq10 ) ) OR ( TITLE-ABS-KEY ( ubiquinone ) ) OR ( TITLE-ABS-KEY ( ubiquinone 10 ) ) OR ( TITLE-ABS-KEY ( 2,3-dimethoxy-5-methyl-6-decaprenylbenzoquinone ) ) ) OR ( ( TITLE-ABS-KEY ( ubidecarenone ) ) OR ( TITLE-ABS-KEY ( ubiquinone 50 ) ) OR ( TITLE-ABS-KEY ( bio-quinone AND q10 ) ) OR ( TITLE-ABS-KEY ( ubisemiquinone AND radical ) ) OR ( TITLE-ABS-KEY ( q-ter ) ) OR ( TITLE-ABS-KEY ( ubisemiquinone ) ) OR ( TITLE-ABS-KEY ( ubiquinol-10 ) ) ) OR ( TITLE-ABS-KEY ( ubiquinol ) ) | 34385 |
| **#3** | ( TITLE-ABS-KEY ( randomized AND controlled AND trial ) OR TITLE-ABS-KEY ( controlled AND clinical AND trial ) OR TITLE-ABS-KEY ( randomized AND controlled AND trials ) OR TITLE-ABS-KEY ( random AND allocation ) OR TITLE-ABS-KEY ( double AND blind AND method ) OR TITLE-ABS-KEY ( single AND blind AND method ) OR TITLE-ABS-KEY ( clinical AND trial ) OR TITLE-ABS-KEY ( clinical AND trials ) OR TITLE-ABS-KEY ( placebos ) OR TITLE-ABS-KEY ( placebo ) OR TITLE-ABS-KEY ( random ) ) | 2825865 |
| **#4** | **#1** AND **#2** AND **#3** | 1591 |

**COCHRANE**

**Number of localized studies:** 333

**Limits:** -

**Number of studies after applying limits:** 333

|  |  |  |
| --- | --- | --- |
|  | **Descriptors** | Number of studies reached |
| **#1** | Me ("Glutathione Reductase") or ("Reductase, Glutathione"):ti,ab,kw or ("Glutathione Peroxidase"):ti,ab,kw or ("Peroxidase Glutathione"):ti,ab,kw or ("Superoxide Dismutase"):ti,ab,kw or ("Dismutase Superoxide"):ti,ab,kw or ("Oxidative Stress"):ti,ab,kw or ("Stress Oxidative"):ti,ab,kw or ("Stress, Oxidative"):ti,ab,kw or ("Total Antioxidant Capacity"):ti,ab,kw or ("Total Antioxidant Status"):ti,ab,kw or ("antioxidant"):ti,ab,kw or ("Oxidant"):ti,ab,kw or ("reactive oxygen species"):ti,ab,kw or ("Catalase"):ti,ab,kw or ("Oxygen Radical Absorbance"):ti,ab,kw or ("reactive nitrogen species"):ti,ab,kw or ("protein carbonyl"):ti,ab,kw or ("lipid peroxide"):ti,ab,kw or ("Total Radical Trapping Antioxidant Parameter"):ti,ab,kw or ("Malondialdehyde"):ti,ab,kw or ("Nitric oxide"):ti,ab,kw or ("8-hydroxydeoxyguanosine"):ti,ab,kw or ("thiobarbituric acid reactive substances"):ti,ab,kw or ("nitrotyrosine"):ti,ab,kw or ("sulfhydryl group"):ti,ab,kw or ("oxidized LDL lipoprotein"):ti,ab,kw or ("xanthine oxidase"):ti,ab,kw or ("paraoxonase-1"):ti,ab,kw | 19279 |
| **#2** | Me ("Coenzyme Q10") or ("Co-enzyme Q10"):ti,ab,kw or ("Coenzyme Q"):ti,ab,kw or ("Q10"):ti,ab,kw or ("CoQ10"):ti,ab,kw or ("Ubiquinone"):ti,ab,kw or ("Ubiquinone 10"):ti,ab,kw or ("2,3-dimethoxy-5-methyl-6-decaprenylbenzoquinone"):ti,ab,kw or ("Ubidecarenone"):ti,ab,kw or ("Ubiquinone 50"):ti,ab,kw or ("Bio-Quinone Q10"):ti,ab,kw or ("Ubisemiquinone radical"):ti,ab,kw or ("Q-ter"):ti,ab,kw or ("Ubisemiquinone"):ti,ab,kw or ("Ubiquinol-10"):ti,ab,kw or ("Ubiquinol"):ti,ab,kw | 1011 |
| **#3** | **#1** AND **#2** | 333 |

**EMBASE**

**Number of localized studies:** 1734

**Limits:** no limits

|  |  |  |
| --- | --- | --- |
|  | **Descriptors** | Number of studies reached |
| **#1** | (('glutathione'/exp OR glutathione) AND ('reductase'/exp OR reductase)) OR (reductase, AND ('glutathione'/exp OR glutathione)) OR (('glutathione'/exp OR glutathione) AND ('peroxidase'/exp OR peroxidase)) OR (('peroxidase'/exp OR peroxidase) AND ('glutathione'/exp OR glutathione)) OR (('superoxide'/exp OR superoxide) AND ('dismutase'/exp OR dismutase)) OR (('dismutase'/exp OR dismutase) AND ('superoxide'/exp OR superoxide)) OR (oxidative AND ('stress'/exp OR stress)) OR (('stress'/exp OR stress) AND oxidative) OR (stress, AND oxidative) OR (total AND ('antioxidant'/exp OR antioxidant) AND ('capacity'/exp OR capacity)) OR (total AND ('antioxidant'/exp OR antioxidant) AND status) OR ('antioxidant'/exp OR antioxidant) OR ('oxidant'/exp OR oxidant) OR (reactive AND ('oxygen'/exp OR oxygen) AND ('species'/exp OR species)) OR ('catalase'/exp OR catalase) OR (('oxygen'/exp OR oxygen) AND ('radical'/exp OR radical) AND ('absorbance'/exp OR absorbance)) OR (reactive AND ('nitrogen'/exp OR nitrogen) AND ('species'/exp OR species)) OR (('protein'/exp OR protein) AND ('carbonyl'/exp OR carbonyl)) OR (('lipid'/exp OR lipid) AND ('peroxide'/exp OR peroxide)) OR (total AND ('radical'/exp OR radical) AND trapping AND ('antioxidant'/exp OR antioxidant) AND ('parameter'/exp OR parameter)) OR ('malondialdehyde'/exp OR malondialdehyde) OR (nitric AND ('oxide'/exp OR oxide)) OR ('8 hydroxydeoxyguanosine'/exp OR '8 hydroxydeoxyguanosine') OR (thiobarbituric AND ('acid'/exp OR acid) AND reactive AND substances) OR ('nitrotyrosine'/exp OR nitrotyrosine) OR (('sulfhydryl'/exp OR sulfhydryl) AND ('group'/exp OR group)) OR (oxidized AND ('ldl'/exp OR ldl) AND ('lipoprotein'/exp OR lipoprotein)) OR (('xanthine'/exp OR xanthine) AND ('oxidase'/exp OR oxidase)) OR ('paraoxonase 1'/exp OR 'paraoxonase 1') | 958552 |
| **#2** | ('coenzyme'/exp OR coenzyme) AND q10 OR ('co enzyme' AND q10) OR (('coenzyme'/exp OR coenzyme) AND q) OR q10 OR coq10 OR 'ubiquinone'/exp OR ubiquinone OR (('ubiquinone'/exp OR ubiquinone) AND 10) OR '2,3 dimethoxy 5 methyl 6 decaprenylbenzoquinone'/exp OR '2,3 dimethoxy 5 methyl 6 decaprenylbenzoquinone' OR 'ubidecarenone'/exp OR ubidecarenone OR (('ubiquinone'/exp OR ubiquinone) AND 50) OR ('bio quinone' AND q10) OR (('ubisemiquinone'/exp OR ubisemiquinone) AND ('radical'/exp OR radical)) OR 'q ter' OR 'ubisemiquinone'/exp OR ubisemiquinone OR 'ubiquinol 10'/exp OR 'ubiquinol 10' OR 'ubiquinol'/exp OR ubiquinol | 37980 |
| **#3** | (randomized AND controlled AND ('trial'/exp OR trial)) OR (controlled AND ('clinical'/exp OR clinical) AND ('trial'/exp OR trial)) OR (randomized AND controlled AND trials) OR (random AND allocation) OR (double AND ('blind'/exp OR blind) AND ('method'/exp OR method)) OR (single AND ('blind'/exp OR blind) AND ('method'/exp OR method)) OR (('clinical'/exp OR clinical) AND ('trial'/exp OR trial)) OR (('clinical'/exp OR clinical) AND trials) OR ('placebos'/exp OR placebos) OR ('placebo'/exp OR placebo) OR (random) | 2423763 |
| **#4** | **#1** AND **#2** AND **#3** | 1734 |

**Appendix B.** Assessment of the risk of bias in the included studies

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Random sequence generation (selection bias)** | **Allocation concealment (selection bias)** | **Blinding of participants and personnel (performance bias)** | **Blinding of outcome assessment (detection bias)** | **Incomplete outcome data (attrition bias)** | **Selective reporting (reporting bias)** | **Other bias** |
| Abdollahzad et al.(2015) | **\_** | **\_** | **\_** | **+** | **?** | **\_** | **\_** |
| Carrasco et al.(2014) | **\_** | **\_** | **?** | **+** | **\_** | **\_** | **?** |
| Dai et al.(2011) | **\_** | **\_** | **\_** | **?** | **\_** | **\_** | **\_** |
| Fakhrabadi et al.(2015) | \_ | **\_** | **\_** | **?** | **\_** | **\_** | **\_** |
| Fallah et al.(2019) | **\_** | **+** | **?** | **+** | **\_** | **?** | **\_** |
| Farhangi et al.(2014) | **?** | **\_** | **\_** | **?** | **\_** | **\_** | **\_** |
| Gholami et al.(2018) | **?** | **+** | **?** | **?** | **\_** | **\_** | **\_** |
| Gholnari et al.(2017) | **\_** | **+** | **?** | **?** | **\_** | **\_** | **\_** |
| Lee et al.(2013) | **?** | **+** | **+** | **+** | **?** | **\_** | **\_** |
| Liu et al.(2016) | **\_** | **\_** | **+** | **+** | **\_** | **\_** | **?** |
| Moazen et al.(2015) | **\_** | **\_** | **+** | **?** | **?** | **\_** | **\_** |
| Mohamadshahi et al.(2014) | **?** | **\_** | **?** | **?** | **?** | **\_** | **\_** |
| Nattagh-eshtivani et al.(2018) | **\_** | **\_** | **\_** | **\_** | **?** | **\_** | **\_** |
| Raygan et al.(2015) | **\_** | **\_** | **\_** | **?** | **\_** | **\_** | **\_** |
| Rodriguez et al.(2015) | **?** | **\_** | **\_** | **?** | **\_** | **\_** | **\_** |
| Singh et al.(2018) | **?** | **\_** | **\_** | **\_** | **?** | **\_** | **\_** |
| Zarei et al.(2018) | **\_** | **+** | **?** | **+** | **\_** | **\_** | **\_** |



A



**Appendix C.** Publication bias of included studies for MDA (A) and TAC (B)