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Influence of germination on the protein content, total phenolic content, and antioxidant capacity of quinoa (*Chenopodium quinoa* Willd.): a systematic review and meta-analysis

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Abstract

Background The germination process has emerged as a promising biotechnological strategy to enhance the nutritional and functional properties of quinoa (*Chenopodium quinoa* Willd.). However, scientific consensus regarding its effects on protein content, total phenolic content, and antioxidant capacity remains limited and controversial.

Objective To systematically review and meta-analysis the scientific evidence on germination effects on protein content, total phenolic content, and antioxidant capacity across white, red, and black quinoa varieties.

Methods A comprehensive literature search was conducted in Scopus, ScienceDirect, and Google Scholar databases (June 2019–March 2025). The MINORS scale was used to judge the level of bias and quality of evidence. Pooled and variety-specific subgroup analyses were performed using ratio of means (ROM) with 95% confidence intervals [95% CI]. Heterogeneity was evaluated through I^2 statistics. Statistical analyses were conducted using R 4.5.0 software.

Results Twenty-one studies met inclusion criteria. Germination significantly increased protein content by ~9% (ROM = 1.09 [95% CI: 1.04–1.14]; $z = 3.789$, $p < 0.001$), with white variety showing the highest increment (~12%). Total phenolic content increased by ~44% (ROM = 1.44 [95% CI: 1.30–1.60]; $z = 6.849$, $p < 0.001$), with red variety exhibiting the greatest enhancement (~51%). Antioxidant capacity improved by ~28% (ROM = 1.28 [95% CI: 1.16–1.42]; $z = 4.729$, $p < 0.001$), with black variety demonstrating superior response (~36%).

Conclusions Germination significantly enhances protein content, total phenolic content, and antioxidant capacity in quinoa, with variety-dependent differential responses that suggest genotype-specific optimization potential.

Limitations Most included studies lacked adequate sample size calculations and consistently employed three replicates, potentially constraining meta-analysis robustness and generalizability of findings.

Keywords Germination, Protein content, Bioactive compounds, Antioxidant capacity, Andean pseudocereals



1 Introduction

Quinoa (*Chenopodium quinoa* Willd.) renowned for its nutritional and functional qualities, this pseudocereal is attracting increasing interest and is currently grown in different regions of the world under a wide range of environmental settings [1]. Originating about 7000 years ago in the Lake Titicaca basin, quinoa was first domesticated there before spreading across South America and subsequently to other parts of the globe [2], it is a crop produced primarily in the Andean region, such as Peru, Bolivia, Chile, Ecuador, Argentina, and Colombia; currently, production has expanded to several countries, achieving a global presence and establishing itself as a superfood [3, 4]. Increasingly recognized worldwide, quinoa stands out for its remarkable grain nutritional quality, which includes a high protein concentration, significant lipid content, and an optimal balance of essential amino acids [2, 5]; in addition, in contrast to traditional cereals, quinoa provides a substantial content of phenolic compounds and antioxidants—including caffeic, ferulic, and vanillic acids—as well as greater concentrations of vitamins (ascorbic acid, thiamin, and α -tocopherol) and essential minerals such as calcium, magnesium, iron, and zinc [6].

Although quinoa grains inherently possess high nutritional value, this can be further enhanced through processing techniques such as germination [7], during the germination process, intercellular enzymes are activated that hydrolyze the nutrients stored in the grain, thus producing numerous physiological and biomolecular changes [8–10]. Evidence indicates that the germination process markedly improves the nutritional properties of both cereals and legumes [11, 12]; in particular, the germination process promotes greater digestibility of both starch and proteins in rice, corn, and barley [13, 14], in addition, the germination process helps diminish antinutritional factors in grains such as cereals and legumes [15, 16]. In the case of quinoa (*Chenopodium quinoa* Willd.), several studies have documented substantial metabolic changes during germination, including the activation of hydrolytic enzymes (amylases, proteases, and phytases) and the synthesis of low molecular weight bioactive compounds [17–19]. These processes improve protein digestibility and the availability index of essential amino acids, while reducing the concentration of saponins, tannins, and phytic acid, compounds traditionally considered antinutritional [20, 21]. Likewise, germination has been shown to significantly increase the content of phenolic compounds and flavonoids, enhancing the total antioxidant capacity of the grain [22, 23]. These changes are associated with the activation of secondary metabolic pathways, particularly those related to shikimic acid metabolism and flavonoid synthesis, which gives germinated quinoa greater functional and nutritional value compared to the raw seed [6, 24]. Overall, germination not only improves nutrient bioavailability but also transforms quinoa into a food with superior functional and antioxidant properties, with potential application in the development of healthy and functional foods [25, 26].

Properly executed systematic reviews and meta-analyses represent the strongest level of evidence in the context of Evidence-Based Medicine (EBM). Their strength lies in the use of rigorous, systematic, and transparent data analysis methods, while meta-analysis specifically combines data from several comparable studies to increase statistical power and provide a more precise overall effect [27].

There are discrepancies in the measurement of outcomes (data) related to the quinoa germination process, including variations in experimental protocols (e.g., temperature

and time) and metrics used, which makes a reliable comparative evaluation difficult. Resolving this existing scientific debate and providing a clear, quantified consensus on the effect of germination is imperative. Currently, there are no published systematic reviews that provide a concrete and quantified overview of the effectiveness of the germination process through meta-analysis. While several individual studies have described the positive effects of germination on the nutritional and functional quality of grains such as quinoa, amaranth, and legumes, these studies vary widely in their methodologies, experimental conditions, and measurement units, making it difficult to draw comparable and generalizable conclusions [17, 24, 28, 29]. In this context, the application of a meta-analysis is presented as a robust and necessary tool to quantitatively integrate existing results, evaluate the consistency of the reported effects, and estimate a weighted average effect [27, 30–33], allowing a more precise determination of the true impact of germination on the nutritional and functional parameters of quinoa.

Meta-analysis has been less widely used in engineering due to methodological heterogeneity, incomplete reporting, low replication, and access barriers [34]. However, it is precisely in highly variable disciplines where a well-designed quantitative synthesis provides the most value, improves precision, reveals patterns, quantifies uncertainty, and fosters reproducible standards. With reporting guidelines of PRISMA 2020 and engineering-specific methodological frameworks, its adoption is feasible and desirable to consolidate evidence and facilitate translation into practice [30, 35, 36].

Therefore, the present study aimed to systematically review the scientific evidence evaluating the effect of the germination process of quinoa (white, red, and black) on protein content, total phenolic content, and antioxidant capacity; using meta-analysis with the ratio of means, in order to synthesize the results of comparative studies (ungerminated and germinated quinoa). This approach provides a comprehensive and statistically robust understanding of the effectiveness of germination across different quinoa varieties.

2 Methods

2.1 Registration of systematic review protocol

The present systematic review and meta-analysis followed the methodological recommendations provided by the *Cochrane Handbook for Systematic Reviews of Interventions* [37] and the *Preferred Reporting Items for Systematic Reviews and Meta-analysis* (PRISMA) statement [38].

2.2 Data sources and search strategies

A systematic literature search was undertaken based on PRISMA recommendations, with dual independent searches conducted by two investigators in three databases [39, 40]. Scopus, ScienceDirect, and Google Scholar databases were searched using a combination of keywords to identify relevant articles from Jun 2019 to March 2025; the searches were limited to the English-language [41]. The search approach was tailored to the specific requirements of each database and executed using title, abstract, and keyword searches:

("malting" OR "malt" OR "germination" OR "malated" OR "sprouts" OR "sprouted" OR "germinated") AND ("quinoa" OR "chenopodium quinoa willd" OR "quinoa") AND

(“phenolic content” OR “antioxidant capacity” OR “bioactive compounds” OR “nutritional components”).

Keywords that were excluded during the literature search: NOT “amaranthus” OR “nutraceutical properties” OR “antinutritional factors”.

Once the eligible studies were identified, data extraction was performed independently by two co-authors, with disagreements resolved through consultation with a third author, as described by Alizadeh et al.⁴². The search ended in August 2025. Records retrieved from the database search were imported into Mendeley (v1.19.8, Elsevier, UK) and processed in Microsoft Excel 2021 (Microsoft Corporation, USA) [43].

2.3 Study selection

Articles were considered eligible if they matched the elements defined by the following study design PICOS: (Population-Intervention-Comparator-Outcomes-Study design) criteria for the eligibility of studies were used to determine the inclusion and exclusion criteria [41, 43].

2.3.1 Population

Scientific articles evaluating the effect of the germination process on the nutritional and functional properties of white, red, or black quinoa.

2.3.2 Intervention

Research that used the germination process (germination only, germination and malting combined, or sprouts only).

2.3.3 Comparator

Control group, where the germination process was not applied

2.3.4 Outcomes

Changes in the values of protein content, total phenolic content and antioxidant capacity

2.3.5 Study design

This systematic review included reports on the efficacy of germination process from an experimental design, with a treatment group (germinated) and a control group (not germinated). Non-randomized experimental or quasi-experimental studies.

2.3.6 Exclusion criteria

(1) Duplicate publications; (2) Incomplete or inaccessible data (articles that do not show the mean, standard deviation and the number of samples evaluated); (3) Literature other than the English-language; (4) Non-experimental design such as reviews, grey literature, conference reports, case reports, theses, etc.; (5) Inconsistency in the outcome metrics or inability to combine data [44].

2.4 Data extraction

First, duplicate publications were removed. Second, titles and abstracts were screened to exclude publications that clearly did not meet the inclusion criteria. Finally, the full text was reviewed to determine the included literature. Extracts included: (1) First author;

(2) Year of publication; (3) Journal name; (4) Initial literature characteristics (including sample size, mean, and standard deviation); (5) Information on quality assessment. This process was completed by two independent researchers and finally verified. In case of discrepancies, a third researcher was consulted [43, 44].

2.5 Risk of bias assessment and methodological quality

Two reviewers independently conducted the risk of bias assessment in line with the methodology described in the *Cochrane Handbook for Systematic Reviews of Interventions* [37]; any inconsistencies were addressed by consulting the senior author [40, 45]. The risk of bias was evaluated using the Methodological Index for Non-Randomized Studies (MINORS), where each item was rated from 0 (not reported), 1 (reported but inadequate), to 2 (reported and adequate), with higher scores reflecting superior methodological quality [46, 47]; twelve criteria were evaluated, with slight modifications for application in engineering studies: (1) A clearly stated aim, (2) Inclusion of consecutive samples, (3) Prospective collection of data, (4) Endpoints appropriate to the aim of the study, (5) Unbiased assessment of the study endpoint, (6) Follow-up period appropriate to the aim of the study, (7) Loss to follow up less than 5%, (8) Prospective calculation of the study size, (9) An adequate control group, (10) Contemporary groups, 11. Baseline equivalence of groups, and 12. Adequate statistical analyses; finally, the risk of bias was reported as: red (high risk of bias), yellow (unclear risk of bias), and green (low risk of bias) [48].

2.6 Statistical analysis

Our meta-analysis of continuous data (protein content, total phenolic content, and antioxidant capacity) was performed using the ratio of means (ROM) and 95% confidence intervals (CI) to measure the effect size of the germination process. Statistical significance was considered as $p \leq 0.05$ [49]. The presence of statistical heterogeneity was assessed using the Cochran Q test, heterogeneity was likely suggested and confirmed if $p \leq 0.05$, quantification of heterogeneity was performed, and values of I^2 ranging 0–24.9%, 25–49.9%, 50–74.9%, and $> 75\%$ were considered as none, low, moderate, and high heterogeneity, respectively [27, 39, 50]. In addition, the overall effect was evaluated [51]. Potential publication bias and small-study effects were evaluated using a combination of visual and statistical approaches [40, 42]. Funnel plots were first visually inspected to assess potential asymmetry between effect sizes and their standard errors [41]. Statistical evidence of funnel plot asymmetry was then examined using Egger's regression test and Begg's rank correlation test, given the limited power of asymmetry tests in meta-analyses with a small to moderate number of studies, a significance threshold of $p \leq 0.10$ was considered indicative of potential asymmetry [52–54]. When evidence of asymmetry was detected or suspected, the trim-and-fill method was applied to estimate the number of potentially missing studies and to assess the impact of such missing studies on the pooled effect size [41], [52–54]. In addition, leave-one-out sensitivity analyses were conducted by sequentially excluding individual studies to evaluate the influence of each study on the overall pooled estimates and to assess the robustness of the results [41, 55]. All analyses were performed using random-effects models. Meta-regression analyses were performed to explore potential sources of between-study heterogeneity, including quinoa variety as a categorical moderator. Mixed-effects models

with REML estimation were used, and the significance of moderators was assessed using the QM test [56–58]. All analysis were performed using packages “metafor” (4.8-0.8) and “meta” (version 8.1-0.1) on R version 4.5.0 [59–62].

3 Results

3.1 Flow of studies through the review

A total of 416 articles were identified through database searches. After excluding 302 duplicates and inaccessible items, 114 articles proceeded to title and abstract screening, with 48 removed at this stage. Full-text assessment was conducted on 66 articles, of which 45 were excluded. Consequently, 21 articles met the inclusion criteria for this review (Fig. 1). Flow diagram was generated using Shiny App R package and ShinyApp for making PRISMA 2020 flow diagrams [63].

3.2 Study characteristics

Of the 21 studies [9, 18, 19, 28, 29, 64–79] included in this review (Table 1), all involved applying the germination process to different quinoa varieties grouped according to their predominant color (white, red, and black); these were evaluated for protein content (27 evaluations involving 180 samples, 90 ungerminated and 90 germinated), total phenolic content (25 evaluations involving 172 samples, 86 ungerminated and 86 germinated), and antioxidant capacity (15 evaluations involving 90 samples, 45 ungerminated and 45 germinated).

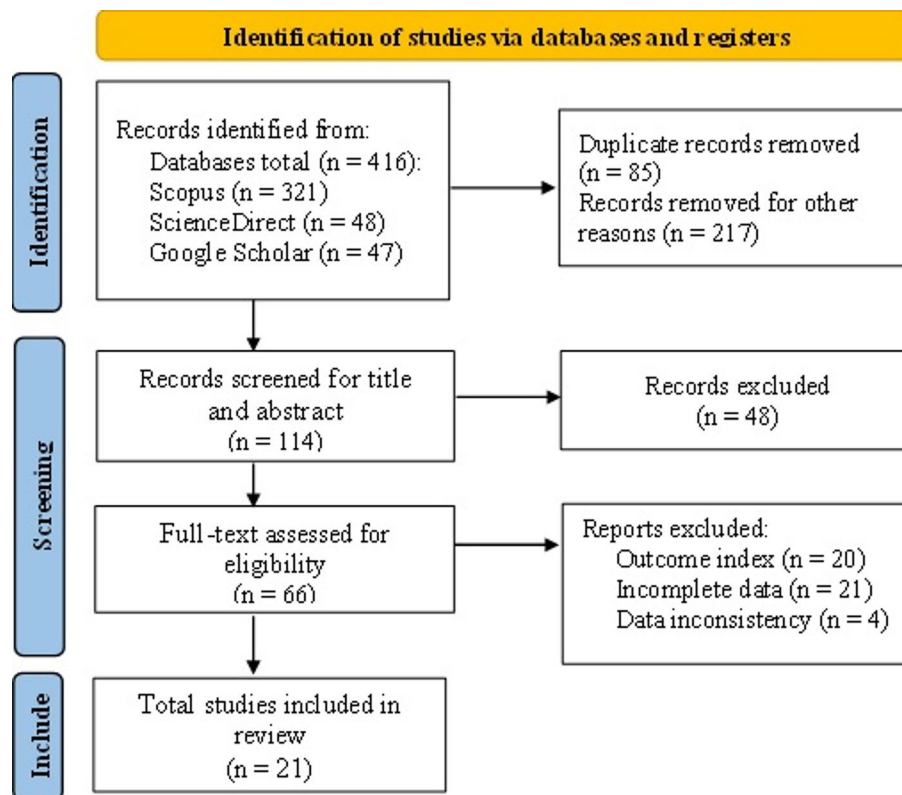


Fig. 1 Preferred reporting Items for systematic reviews and meta-analyses (PRISMA) flow chart illustrating different phases of the search and study selection

Table 1 Summary of included studies

Study	Group (color)/variety			Germination process	Outcomes		
	White	Red	Black		Protein	Total phenolic content	Anti-oxidant capacity
Aguilar et al. 2019 [9]	INIA Salcedo	Pasank-alla Roja	Negra Collana	Germinated at 25 °C for 48 h, moisture 45–55%.	Content (%)	GAE.100 ⁻¹ g	DPPH (% inhibition)
Almaguer et al. 2023 [64]	DS	–	–	Germination moisture to 46%, temperature 16 °C and time 6 days (144 h).	Content (%)	–	–
Al-Qabba et al. 2020 [65]	–	DS	–	Germination moisture 90–93% at 17 °C during 9 days (216 h).	–	mg GAE 100 g ⁻¹	mmol TE 100 g ⁻¹
Altıkardeş and Güzel, 2024 [66]	DS	–	–	Pre-germination by ultrasound, subsequent germination at 25 °C for 72 h, moisture NR.	–	mg GAE 100 g ⁻¹	–
Bhinder et al. 2021 [67]	DS	–	DS	Hydrated for 4 h at 25 °C, germinated at 24 °C for 72 h, moisture 45–55%.	Content (%)	mg GAE/g	DPPH (μmol/g)
Choque-Quispe et al. 2021 [18]	INIA Salcedo	Pasank-alla Roja	Negra Collana	Germinated at 35 °C for 48 h, moisture 43–45%.	Content (%)	mg GAE/100 g	DPPH (μmol TE/g)
Demir and Bilgiçli, 2021 [68]	DS	–	–	Germinated at 20 °C for 48 h, moisture NR.	Content (%)	mg GAE/g	–
Dostalíková et al. 2024 [69]	DS	–	–	Germinated at 16 °C for 4 days (96 h), moisture NR.	Content (%)	–	–
Franco et al., 2021 [70]	DS	–	–	Soaked for 2 h at 20 °C, germinated at 25 °C for 24 h, moisture NR.	Content (%)	–	–
Guardianelli et al. 2022 [71]	Royal	Royal	–	Germinated to 20 °C for 48 h, moisture NR.	–	mg GAE/100 g	DPPH (mg/μL)
Kewuyemi et al. 2022 [72]	DS	–	–	Soaked at 28 °C for 24 h, incubated germinated at 28 °C for 48 h, moisture NR.	Content (%)	mg GAE/g	DPPH (%)
Khan et al. 2025 [79]	JQ-778	–	–	Germinated at 25 °C for 96 h, moisture NR.	Content (%)	mg GAE/100 g	DPPH (%)
Ma et al. 2021 [78]	DS	DS	DS	Germinated at 20 °C under dark for 4 days (96 h), moisture NR.	Content (%)	mg g ⁻¹	–
Prasad et al. 2023 [73]	DS	–	–	Soaked for at 28 °C for 8 h, germinated at 28 °C for 48 h, moisture NR.	Content (%)	mg GAE/100 g	–
Ramos-Pacheco et al. 2024 [19]	Choclito	Pasank-alla Roja	Negra Collana	Soaked at 20 °C for 4 h, germinated at 25 °C for 72 h, moisture ~95%.	Content (%)	–	–
Ramos-Pacheco et al. 2025 [28]	Señor del huerto	Pasank-alla Roja	Negra Collana	Soaked at 20 °C for 4 h, germinated at 25 °C for 72 h, moisture ~40%.	Content (%)	GAE/100 g	DPPH (μmol TE/g)
Suárez-Estrella et al. 2021 [74]	Titicaca	–	–	Germinated to 22 °C for 72 h, moisture ~93%.	–	mg GAE/g	–

Table 1 (continued)

Study	Group (color)/variety			Germination process	Outcomes		
	White	Red	Black		Protein	Total phenolic content	Anti-oxidant capacity
Thakur et al. 2021 [75]	DS	–	–	Germinated at 25 °C for 72 h, moisture NR.	Content (%)	mg GAE/100 g	–
Vento et al. 2024 [29]	ECU 0621	–	–	Germinated to 37 °C for 2 days (48 h), moisture NR.	–	mg GAE/g	–
Yarabbi et al. 2023 [76]	DS	–	–	Soaked for 24 h, after, germinated to 35% humidity at 21 °C for 48 h.	Content (%)	–	–
Younis et al. 2024 [77]	DS	–	–	Germinated at 15 °C for 5 days (120 h), moisture NR.	Content (%)	–	–

DS: Indicates color but does not specify variety; NR: Not reported. Quantitative information before and after germination is shown in Figs. 5 and 6, and 7

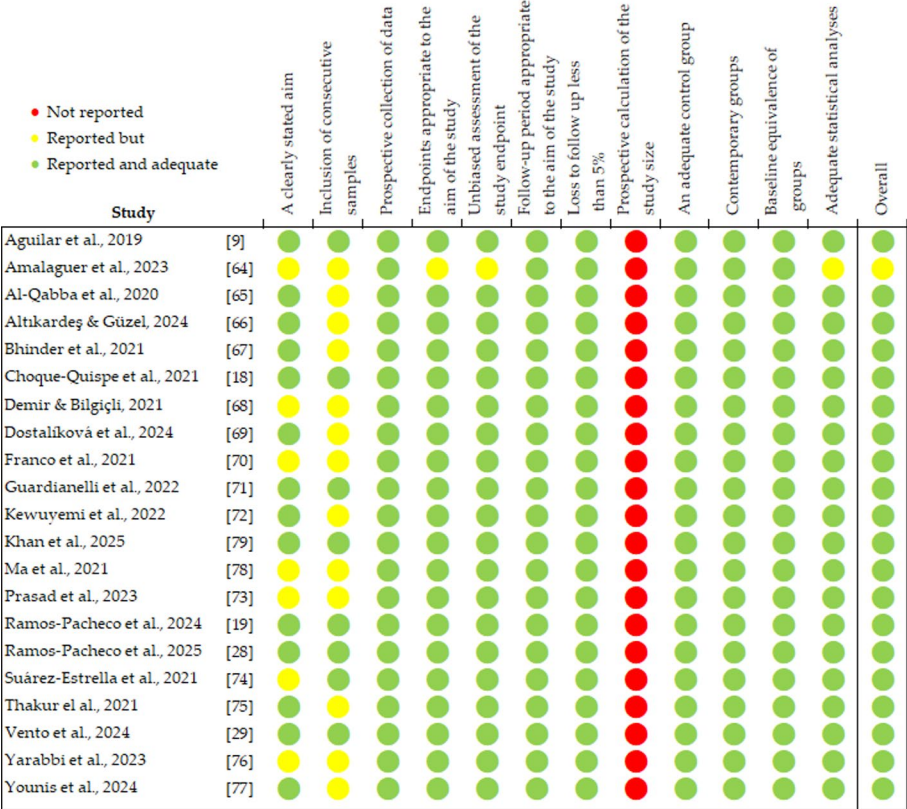


Fig. 2 Traffic plot to risk of bias assessment with Methodological Index for Non-Randomized Studies (MINORS) plot, each item is scored on a scale of 0 (red = not reported), 1 (yellow = reported but inadequate), and 2 (green = reported and adequate)

3.3 Quality assessment of the included literature

A summary of the risk of bias assessment with *Methodological Index for Non-Randomized Studies* (MINORS) is show in Fig. 2, each item was scored on a scale of 0 (red = not reported), 1 (yellow = reported but inadequate), and 2 (green = reported and adequate); with a higher score indicated better methodological quality; overall, all studies were

found to be reported and adequate for inclusion in this review [9, 18, 19, 28, 29, 65–79]; the study conducted by Almaguer et al. ⁶⁴ was the only one with an overall rating of reported but inadequate. It was evident (Fig. 3) that all studies presented a high risk of bias in the “*prospective calculation of the study size*” category; likewise, in most categories of the MINORS scale, the studies included in this review presented a low risk of bias; except in the categories “*clearly stated aim*” and “*inclusion of consecutive samples*” where 33% and 62% of the studies presented an unclear risk of bias, respectively.

3.4 Meta-analysis with ratio of means

3.4.1 Protein content

The germination process significantly increased the protein content of quinoa (pooled varieties), as shown in Fig. 4 (test for overall effect: $z = 3.789$; $p \leq 0.05$, $p = 0.000$) on the protein content of quinoa (pooled varieties), increasing it by ~9% (ratio of means 1.09 [95% CI, 1.04 to 1.14]); high heterogeneity was evident in the values reported in the studies ($I^2 = 99.98\%$, $p \leq 0.05$, $p = 0.000$). Regarding the subgroup analysis (black, red, and white quinoa), the black variety increased the protein content by ~4% (ratio of means 1.04 [95% CI, 0.97 to 1.12]), with high heterogeneity ($I^2 = 99.07\%$, $p \leq 0.05$, $p = 0.000$); the red variety increased by ~5% (ratio of means 1.05 [95% CI, 0.98 to 1.13]), with high heterogeneity ($I^2 = 99.84\%$, $p \leq 0.05$, $p = 0.000$); finally, the white variety increased by ~12% (ratio of means 1.12 [95% CI, 1.05 to 1.20]); with high heterogeneity ($I^2 = 99.99\%$, $p \leq 0.05$, $p = 0.000$); this last variety showed a greater increase compared to the other varieties; there was no difference between subgroups (test for subgroup differences, $p > 0.05$, $p = 0.241$).

3.4.2 Total phenolic content

As shown in Fig. 5, germination markedly enhanced the total phenolic content in quinoa (test for overall effect: $z = 6.849$; $p \leq 0.05$, $p = 0.000$) on the total phenolic content of quinoa (pooled varieties), increasing it by ~44% (ratio of means 1.44 [95% CI, 1.30 to 1.60]); high heterogeneity was evident in the values reported in the studies ($I^2 = 99.91\%$, $p \leq 0.05$, $p = 0.000$). Regarding the subgroup analysis (black, red, and white quinoa), the black variety increased the total phenolic content by ~45% (ratio of means 1.45 [95% CI, 1.10 to 1.92]), with high heterogeneity ($I^2 = 99.64\%$, $p \leq 0.05$, $p = 0.000$); the red variety increased by ~51% (ratio of means 1.51 [95% CI, 1.15 to 1.97]), with high heterogeneity ($I^2 = 99.94\%$, $p \leq 0.05$, $p = 0.000$); finally, the white variety increased by ~41% (ratio of means 1.41 [95% CI, 1.25 to 1.60]); with high heterogeneity ($I^2 = 99.92\%$, $p \leq 0.05$,

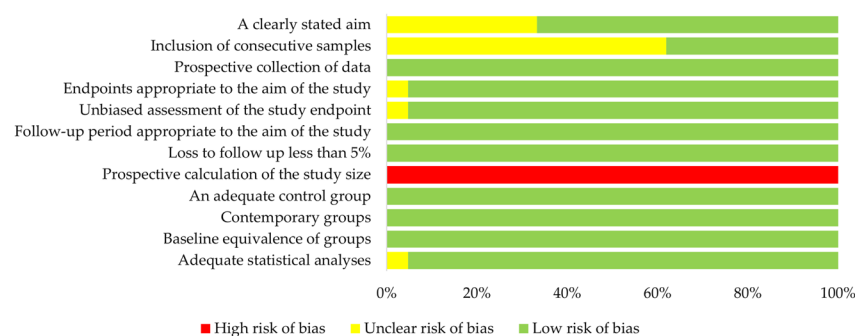


Fig. 3 Assessment of the risk of bias of the studies

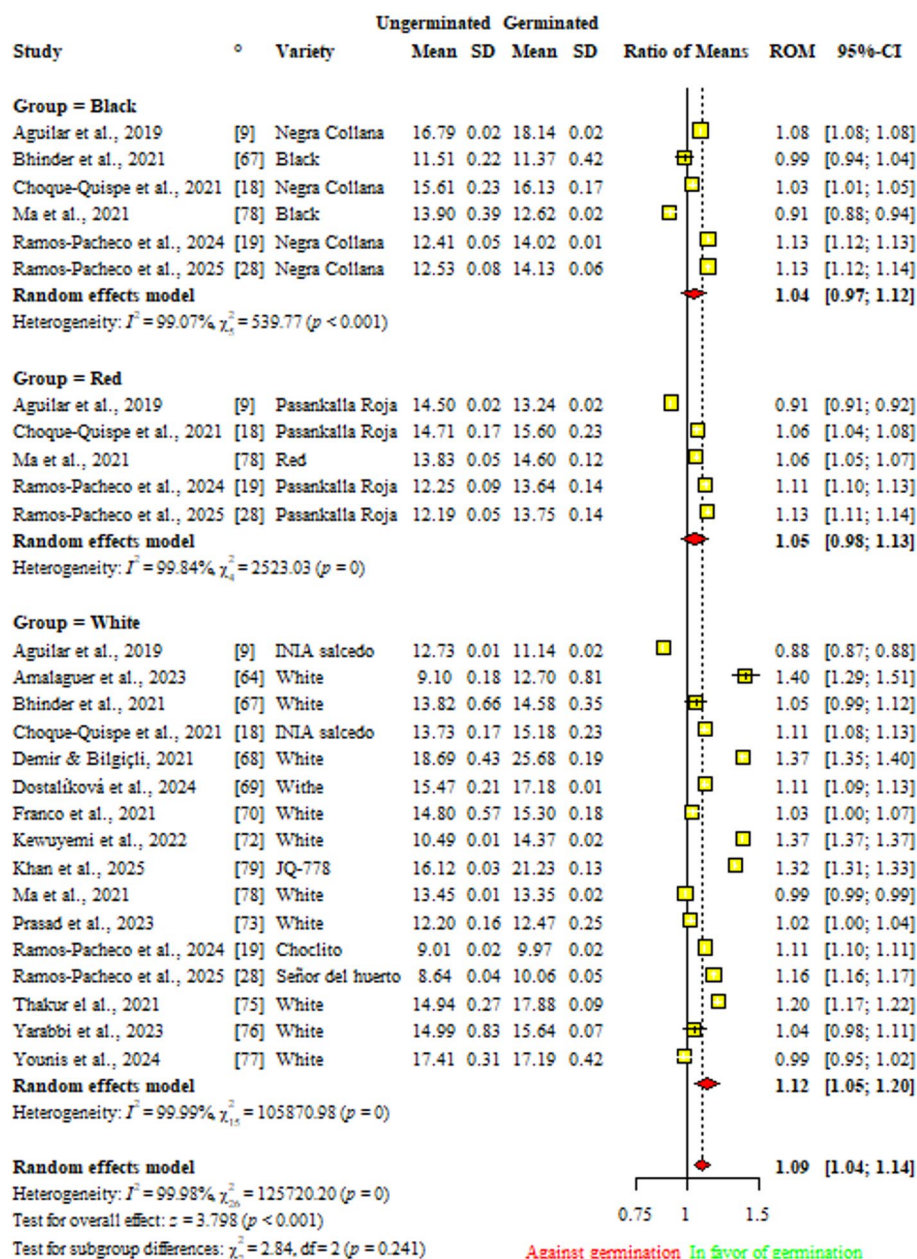


Fig. 4 Forest plot for the evaluation of the effect of germination on the protein content of white, red and black quinoa

$p = 0.000$); the red variety showed a greater increase compared to the other varieties; there was no difference between subgroups (test for subgroup differences, $p > 0.05$, $p = 0.908$).

3.4.3 Antioxidant capacity

Figure 6 illustrates that the germination process also produced a significant increase in antioxidant capacity across quinoa varieties (test for overall effect: $z = 4.729$; $p \leq 0.05$, $p = 0.000$) on the antioxidant capacity of quinoa (pooled varieties), increasing it by $\sim 28\%$ (ratio of means 1.28 [95% CI, 0.16 to 1.42]); high heterogeneity was evident in the values reported in the studies ($I^2 = 99.79\%$, $p \leq 0.05$, $p = 0.000$). Regarding the subgroup analysis

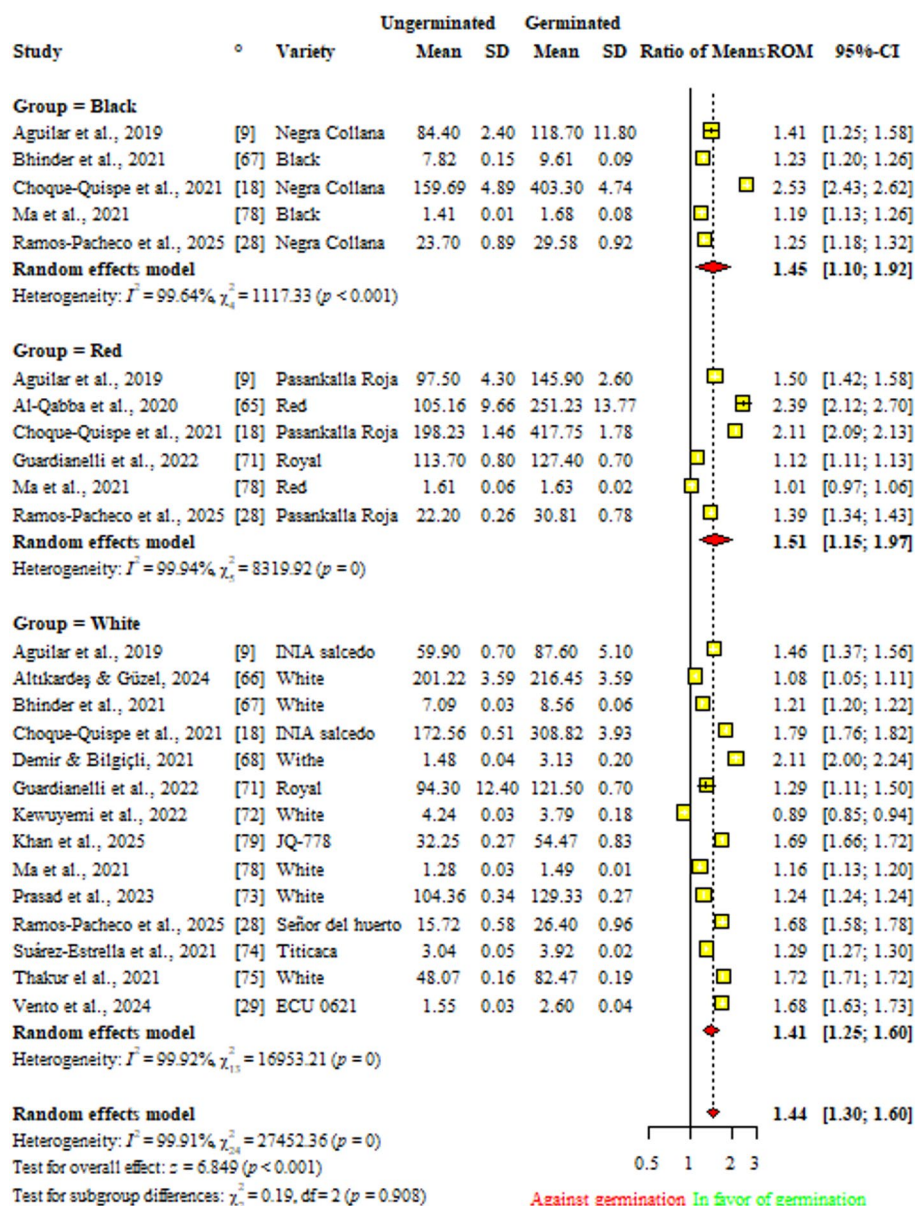


Fig. 5 Forest plot for the evaluation of the effect of germination on the total phenolic content of white, red and black quinoa

(black, red, and white quinoa), the black variety increased the antioxidant capacity by $\sim 36\%$ (ratio of means 1.36 [95% CI, 1.14 to 1.61]), with high heterogeneity ($I^2 = 99.61\%$, $p \leq 0.05$, $p = 0.000$); the red variety increased by $\sim 26\%$ (ratio of means 1.26 [95% CI, 1.13 to 1.41]), with high heterogeneity ($I^2 = 88.46\%$, $p \leq 0.05$, $p = 0.000$); finally, the white variety increased by $\sim 23\%$ (ratio of means 1.23 [95% CI, 0.99 to 1.53]); with high heterogeneity ($I^2 = 99.91\%$, $p \leq 0.05$, $p = 0.000$); the black variety showed a greater increase compared to the other varieties; there was no difference between subgroups (test for subgroup differences, $p > 0.05$, $p = 0.660$).

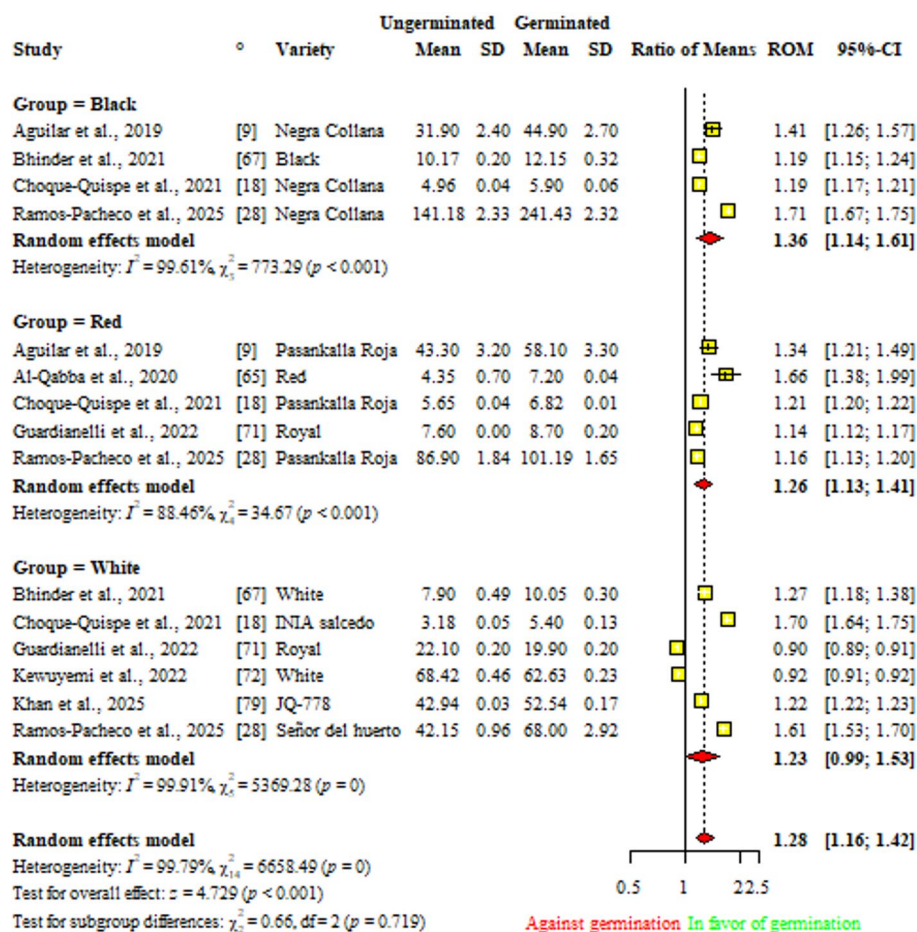


Fig. 6 Forest plot for the evaluation of the effect of germination on the antioxidant capacity of white, red and black quinoa

3.5 Publication bias

Figure 7 shows the funnel plot analysis for protein content (a), total phenolic content (b), and antioxidant capacity (c); in the present review, a slight asymmetry was observed in the funnel plot; most studies presented effect sizes greater than the pooled effect size [80, 81], potential publication bias was assessed using Egger's regression test and Begg's rank correlation test [42, 52, 54]. Egger's test did not indicate funnel plot asymmetry for protein content ($p > 0.10$; $p = 0.807$) or total phenolic compounds ($p > 0.10$; $p = 0.638$), while a marginally significant result was observed for antioxidant capacity ($p \leq 0.10$; $p = 0.058$) [41]. In contrast, Begg's test did not reveal significant asymmetry (association between effect sizes and their standard errors) for protein content ($p > 0.10$; $p = 0.134$), total phenolic compounds ($p > 0.10$; $p = 0.502$), and antioxidant capacity ($p > 0.10$; $p = 0.559$).

To further explore the potential impact of small-study effects, the trim-and-fill method was applied to antioxidant capacity (see supplementary material) [41, 54, 82]. This analysis suggested the presence of three potentially missing studies on the left side of the funnel plot ($k_0 = 3$; $SE = 2.83$), resulting in a reduction of the pooled effect size from Log 0.25 (1.28) to Log 0.15 (1.16) from ~28% to ~16% approximately; however, the test for missing studies was not significant ($p > 0.05$; $p = 0.063$), indicating that evidence for publication bias was suggestive but not conclusive [52, 53]. Additionally, leave-one-out sensitivity analyses showed that the pooled effect was not driven by any single study, with

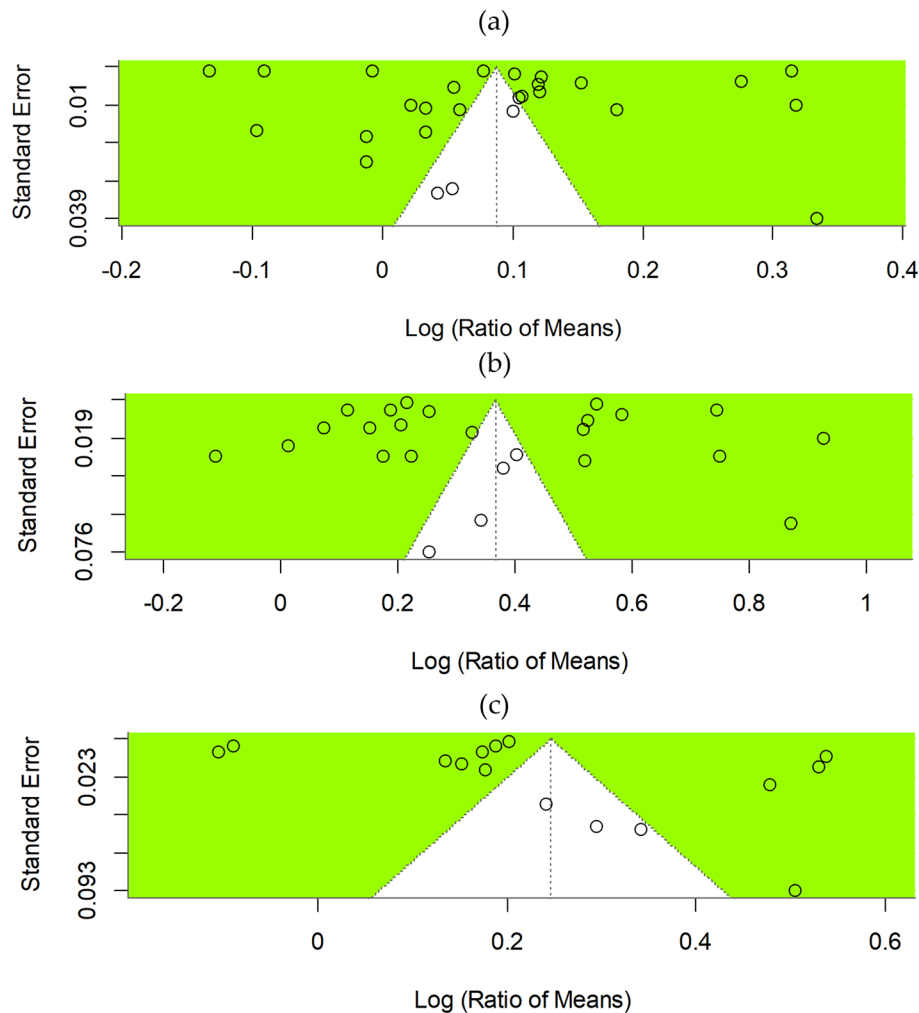


Fig. 7 Funnel plot analysis: **a** protein content, **b** total phenolic content, and **c** antioxidant capacity

no substantial changes in the overall estimate following the sequential exclusion of individual studies [41, 55]. Overall, these analyses suggest that the pooled results are robust, although the magnitude of the effect for antioxidant capacity should be interpreted with caution.

Given the substantial heterogeneity observed between the studies, a meta-regression analysis was performed to assess whether the quinoa variety explains some of the variability between the studies.

3.6 Meta-regression to explore potential sources of between-study heterogeneity with reference to the quinoa variety as a moderator

Meta-regression analyses were conducted to examine whether quinoa variety explained between-study heterogeneity in protein content [56–58, 83]. The test of moderators was statistically significant ($QM(df=3)=16.98$, $p=0.001$), indicating that varietal differences contributed to the observed heterogeneity. Among the varieties, only white quinoa showed a statistically significant positive association with protein content ($p \leq 0.05$, $p=0.000$), whereas the effects for black ($p > 0.05$, $p=0.394$) and red quinoa ($p > 0.05$, $p=0.345$) were not significant. Despite the inclusion of this moderator, substantial

residual heterogeneity remained ($QE(df=24)=108933.78$, $p=0.000$), suggesting that additional unmeasured factors may influence protein content across studies.

For total phenolic compounds, meta-regression revealed a strong moderating effect of quinoa variety ($QM(df=3)=43.63$, $p=0.000$). All three varieties were significantly associated with higher phenolic content, with positive and statistically significant effects observed for black ($p\leq 0.05$, $p=0.003$), red ($p\leq 0.05$, $p=0.000$), and white quinoa ($p\leq 0.05$, $p=0.000$). These results indicate that varietal differences account for a meaningful proportion of the between-study variability. However, significant residual heterogeneity persisted after accounting for variety ($QE(df=22)=26390.45$, $p=0.000$), implying that other study-level characteristics may also contribute to variability in phenolic content.

Meta-regression analysis demonstrated that quinoa variety significantly moderated antioxidant capacity ($QM(df=3)=20.62$, $p=0.000$). Significant positive associations were observed for white ($p\leq 0.05$, $p=0.016$), black ($p\leq 0.05$, $p=0.004$), and red quinoa ($p\leq 0.05$, $p=0.011$), indicating consistent varietal differences across studies. Nevertheless, residual heterogeneity remained high after inclusion of the moderator ($QE(df=12)=6177.25$, $p=0.000$), suggesting that additional factors beyond quinoa variety may influence antioxidant capacity.

Overall, meta-regression analyses indicated that quinoa variety was a major source of heterogeneity between studies in terms of protein content, total phenolic compounds, and antioxidant capacity, supporting a biological (variety) explanation for part of the observed variability across studies.

4 Discussion

Our systematic review and meta-analysis provide robust evidence for the effectiveness of the germination process on protein content, total phenolic content, and antioxidant capacity using evaluation with ratio of means, which is a tool used when measurement units are reported in different scale, allowing the comparison of data across different measures [27, 49]. To our knowledge, this is the first systematic review and meta-analysis, adapting this tool (widely used in health sciences) for use in systematic reviews in the engineering field. Our meta-analysis quantitatively reports on the effects of the germination process on quinoa; our research results contribute to clarifying the efficacy of this process. The synthesis of the available literature facilitates a better understanding of the methods employed and the identification of research gaps and future challenges.

In our meta-analysis, 21 studies were included, where in the evaluation of the risk of bias according to the MINORS rating scale, the biggest problem present in the reviewed and included studies was the “*prospective calculation of the study size*”, this is because in experimental studies carried out in the field of engineering, the calculation of the sample number is not carried out adequately or is not reported and there is always a tendency to use 3 replicas for each treatment [84–88].

With reference to the high heterogeneity ($I^2 > 75\%$) in our meta-analysis, this is due to the fact that in the publications of experimental research in the engineering branch, in the included studies there are considerable variations in the experimental processes [89, 90]; as in the case of germination research where time, temperature, moisture, drying and/or roasting, etc. vary [9, 17], in addition to different measurement and analysis processes and techniques, thus reflecting that the estimated effects vary significantly

between different studies, which leads to these studies evaluated in an engineering meta-analysis presenting high heterogeneity [32, 89, 91]. This high heterogeneity is largely due to the wide disparity in operational protocols; for example, germination time varied from 24 h to 9 days, and temperature spanned 16 °C to 37 °C. This lack of standardization has a direct biological basis, as these operational factors critically influence enzymatic activity (proteases, polyphenol oxidases) and the kinetics of secondary metabolite synthesis. Therefore, the magnitude of the germination effect is highly dependent on the protocol employed. Given the high heterogeneity, the random-effects model was the most appropriate compared to the fixed-effects model, considering that the true effects varied among the included studies [27, 49], furthermore, the meta-analysis was also conducted by subgroups (white, red, and black quinoa); besides, to the pooled effect.

The results of our meta-analysis confirm that quinoa germination is a dynamic process that significantly modifies protein fractions, with effects dependent on the variety and processing conditions. Regarding protein content, germination resulted in an average increase of ~9% across pooled quinoa varieties, with white quinoa exhibiting the highest increment (~12%), followed by red (~5%) and black (~4%). This varietal response is closely associated with structural differences in the seed coat and embryo permeability, which influence water uptake and early activation of proteolytic enzymes [92]. While white quinoa benefits from faster imbibition and protease activation, the thicker pericarp characteristic of black quinoa may delay these processes, partially explaining its attenuated response. Nevertheless, protein reductions reported in some studies highlight the dual role of proteolysis and amino acid leaching during prolonged germination, reinforcing the need of optimized process [9, 66].

With respect to total phenolic content (TPC), germination induced a substantial increase of ~44% across pooled varieties, with red quinoa showing the most pronounced enhancement (~51%), followed by black (~45%) and white (~41%). This differential response reflects both *de novo* synthesis and the release of bound phenolics during germination. The increase in TPC is primarily driven by the activation of the phenylpropanoid pathway, mediated by key enzymes such as phenylalanine ammonia-lyase (PAL), 4-coumarate-CoA ligase (4CL), chalcone synthase (CHS), and chalcone isomerase (CHI), which catalyze the biosynthesis of phenolic acids and flavonoids [93, 94].

In red quinoa, the magnitude of the TPC increase appears to be linked to a higher basal content of pigmented phytochemicals, including flavonoids and betalains, as well as a greater sensitivity of PAL activity to germination stimuli. Under controlled germination conditions (20–25 °C for 24–72 h), enzymatic depolymerization of cell wall components facilitates the release of phenolics previously bound to polysaccharides and proteins, while simultaneously promoting the synthesis of new metabolites [71, 95, 96]. This response is particularly pronounced in red quinoa, which has been reported to preferentially accumulate ferulic acid and quercetin derivatives as part of an enhanced antioxidant defense during early sprouting [65, 97–99]. In contrast, the increase observed in black and white quinoa is more strongly associated with the enzymatic liberation of bound phenols via esterases and glucosidases, rather than extensive *de novo* biosynthesis [65, 74].

Although antioxidant capacity increased by ~28% overall after germination, the magnitude of this response was clearly variety-dependent, with black quinoa exhibiting the strongest enhancement (~36%), followed by red (~26%) and white (~23%) varieties.

This pattern is associated with the accumulation of phenolic compounds and flavonoids, the presence of low-molecular-weight antioxidants, and the activation of key antioxidant enzymes such as superoxide dismutase, peroxidase, catalase, and glutathione reductase [79, 100–102]. The superior response of black quinoa is attributed to its higher concentration of bioactive metabolites in the seed coat, including alkaloids, tannins, terpenoids, epicatechin derivatives, and γ -aminobutyric acid (GABA), which collectively enhance radical-scavenging activity [95, 103, 104]. Previous studies reporting increases of up to ~40% in Negra Collana and ~34% in Pasankalla Roja support these findings [9, 18, 28]. In contrast, the lower response of red and white quinoa appears to reflect qualitative differences in phenolic profiles rather than total concentration, while prolonged germination may reduce antioxidant capacity due to compound degradation and leaching [65, 77].

The interaction between quinoa variety and germination time plays a critical role in shaping nutritional and functional outcomes. During the first 36 h of germination, structural relaxation of the cell wall and initial protein mobilization predominate, favoring amino acid accumulation, particularly in white quinoa due to its higher water absorption capacity [105]. The 48–72 h interval represents an optimal metabolic window, during which enzymatic activity maximizes mineral bioavailability, phenolic accumulation, and antioxidant capacity while reducing antinutritional factors such as phytic acid and saponins [19, 106]. Beyond 72 h, although certain metabolites such as GABA and ascorbic acid may continue to increase, overall nutritional quality may decline due to excessive catabolism and leaching, reinforcing 48–72 h as the most efficient processing range, particularly for pigmented varieties.

In the funnel plot for the studies included in our review with meta-analysis, the dispersion in the effect size (log ratio of means) was due to the high variability between studies, especially in studies with a higher standard error [107]; this dispersion is expected when there are relevant methodological or population differences between studies, and when the sample sizes are small [33]; statistically, no asymmetry was evident to content protein and total phenolics compounds; while a marginally significant of asymmetry was observed for antioxidant capacity. Therefore, for antioxidant capacity, when applying the trim and fill analysis, it indicated a reduction in the pooled effect size, the adjusted estimate remained positive, and the evidence from missing studies was marginal; along with the lack of confirmation by the Begg test and the leave-one-out sensitivity test, these findings suggest that the observed asymmetry is unlikely to be solely due to publication bias. There is no widespread evidence of publication bias for protein content and total phenolic compounds; only antioxidant capacity shows weak indications of asymmetry, overall results are robust and consistent [52, 55, 82].

The significant moderating role of quinoa variety suggests that part of the observed heterogeneity—and the marginal funnel plot asymmetry for antioxidant capacity [56–58, 83]—may reflect genuine varietal differences rather than publication bias alone [18, 19, 28].

To ensure methodological transparency and analytical rigor, it is essential to clearly articulate the study's limitations. These include the persistence of high residual heterogeneity (I^2), which primarily stems from the lack of standardized germination protocols across laboratories, significantly complicating direct data comparison. Furthermore, the inclusion of only 21 studies restricts the statistical power necessary for executing

advanced meta-regressions. Finally, a critical limitation is the deficiency in reporting key experimental variables—such as humidity or aeration—in the primary literature, which prevents their inclusion as essential covariates in the quantitative synthesis to fully explain the observed variance.

Our meta-analysis reveals that germination is an effective strategy for enhancing the nutritional and functional value of quinoa, although the benefits depend on the variety, germination time, and processing conditions applied. In practice, white quinoa appears to be the most promising for increasing protein content, red quinoa the most efficient in accumulating phenolic content, and black quinoa the most antioxidant capacity. These results suggest the need for a varietal approach in the design of functional foods and quinoa-derived products, opening up opportunities for innovation in the food industry geared toward consumers who demand natural ingredients with healthy properties.

5 Conclusion

This meta-analysis suggests that the germination process significantly improves the protein content, total phenolic content, and antioxidant capacity of white, red, and black quinoa, respectively.

Protein content is increased by enzymatic hydrolysis (maximized in white quinoa), while the bioactive value and antioxidant capacity are increased by the synthesis and release of phenolic content (maximized in red and black quinoa) with these responses being strongly variety-dependent and influenced by germination process.

These findings provide evidence-based guidance for the food industry, supporting the selection of a quinoa variety specifically aligned with the desired nutritional or functional end-product.

Abbreviations

ARA%	Ascorbic acid reducing activity percentage
CAT	Catalase
CHI	Chalcone isomerase
CHS	Chalcone synthase
CI	Confidence interval
DS	Variety not specified (Doesn't Specify)
NR	Not reported
DPPH	2,2-diphenyl-1-picrylhydrazyl
EBM	Evidence-Based Medicine
GAE	Gallic Acid Equivalents
GR	Glutathione reductase
I^2	I-squared statistic (heterogeneity index)
MINORS	Methodological Index for Non-Randomized Studies
PAL	Phenylalanine ammonia-lyase
POD	Peroxidase
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
R	R statistical software
ROM	Ratio of means
SD	Standard deviation
SOD	Superoxide dismutase
TE	Trolox Equivalents
4CL	4-coumarate-CoA ligase
TPC	Total phenolics compounds

Supplementary Information

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Supplementary Material 1.

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Author contributions

Author Contributions: Jesús Obregón-Domínguez: senior author, writing – review and editing, writing – original draft, data visualization, project management, research, formal analysis, meta-analysis, meta-regression. Gilbert Rodríguez: evaluation of the articles and editing. Augusto Castillo: validation, supervision, resources and methodology. Carlos Ruiz Padilla: supervision, conceptualization. William Vera: literature search and data collection, writing, review and editing. All authors have read and agreed to the published version of the manuscript.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable. This systematic review and meta-analysis doesn't involve the use of humans or animals in our research studies. Not applicable. This systematic review and meta-analysis doesn't involve humans participants.

Clinical trial number

Not applicable for systematic review and meta-analysis.

Consent for publication

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Competing interests

The authors declare no competing interests.

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