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Review

Potato Biofortification: A Systematic Literature Review on Biotechnological Innovations of Potato for Enhanced Nutrition

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Abstract: Potato biofortification is a comprehensive approach aimed at enhancing the nutritional content of potatoes, addressing widespread nutrient deficiencies and contributing to global food security. This systematic review examines the existing literature on various aspects of potato biofortification, encompassing genetic, agronomic, and biotechnological strategies. The review highlights the nutritional significance of potatoes, emphasizing their role as a staple food in many regions. Genetic approaches to biofortification involve the identification and use of natural variations in potato germplasm to develop varieties with elevated levels of essential nutrients. This includes targeting key micronutrients, such as iron, zinc, and vitamins, through traditional breeding methods. The review explores the genetic diversity within potato germplasm and the potential for breeding programs to develop nutrient-rich varieties. Agronomic practices play a crucial role in potato biofortification, with studies demonstrating the impact of tuber priming and the application of mineral fertilizers on nutrient concentrations in potatoes. The review delves into the intricacies of agronomic biofortification, emphasizing the importance of precise dosages and timing for optimal results. Biotechnological tools, including transgenic and non-transgenic approaches, are discussed in the context of potato biofortification. The review evaluates the efficiency and ethical considerations associated with the development of biofortified transgenic potatoes and emphasizes the significance of non-transgenic approaches in addressing consumer concerns and regulatory barriers. Overall, this systematic review provides a comprehensive overview of the current state of potato biofortification research. It synthesizes findings from diverse studies, offering insights into the potential of biofortified potatoes to address hidden hunger and contribute to improved nutritional outcomes. This review also identifies knowledge gaps and areas for future research, guiding the direction of efforts to harness the full potential of potato biofortification for global food and nutrition security.

Keywords: agronomic breeding; nutrient content; CRISPR; transgenic approach

Citation: Agrawal, S.; Kumar, A.; Gupta, Y.; Trivedi, A. Potato Biofortification: A Systematic Literature Review on Biotechnological Innovations of Potato for Enhanced Nutrition. *Horticulturae* **2024**, *10*, 292. https://doi.org/10.3390/horticulturae10030292

Academic Editor: Massimiliano Renna

Received: 2 February 2024
Revised: 4 March 2024
Accepted: 8 March 2024
Published: 19 March 2024

1. Introduction

Nutritional security refers to the assurance that all individuals and communities have access to a sufficient and balanced supply of nutritious food to meet their dietary needs and lead healthy lives. It goes beyond mere food availability, encompassing factors such as accessibility, use, and stability of food sources. Achieving nutritional security requires addressing issues like poverty, food distribution systems, education, and health infrastructure to ensure that people not only have enough food but also access diverse and nutrient-rich options. This concept emphasizes the importance of promoting sustainable and equitable food systems to combat malnutrition and enhance overall well-being on a global scale [1]. Nutritional security and malnutrition are closely correlated, as nutritional security aims to prevent and alleviate malnutrition. Malnutrition is a condition that results from an imbalance between the body's nutrient requirements and its intake. Nutritional security seeks to ensure that individuals and communities have access to a diverse and balanced diet, addressing both the quantity and quality of food to prevent various forms of malnutrition [2]. When nutritional security is compromised, it can lead to malnutrition in different forms, such as undernutrition, overnutrition, and micronutrient deficiencies. Undernutrition, which includes conditions like stunting, wasting, and being underweight, often results from insufficient access to food and essential nutrients. On the other hand, overnutrition, characterized by obesity and related health issues, can occur when people have access to energy-dense but nutrient-poor diets. Efforts to enhance nutritional security involve addressing the root causes of malnutrition, including poverty, inadequate healthcare, and insufficient education about nutrition.

Additionally, there is a widespread issue of micronutrient malnutrition leading to "hidden hunger", particularly in developing nations. The deficiency of essential vitamins and minerals has become a significant global health concern, affecting over 2 billion people worldwide [3,4]. In low- and middle-income countries, about one-third of children aged 6–59 months experience vitamin A (Retinol) deficiency, and 18% suffer from iron deficiency. Key deficiencies impact roughly 30% of the population, including 60% for zinc, 60% for iron, 15% for selenium, and 30% for iodine [5]. However, a looming challenge is the projected global population surpassing 9 billion people by 2050, placing immense pressure on agriculture to adequately feed this growing population [6].

By ensuring access to diverse, nutritious foods and promoting sustainable food systems, nutritional security becomes a key strategy in combating malnutrition and improving overall health outcomes [7]. However, a substantial number of individuals, as reported by the World Health Organization in 2021, still suffer from hunger, reaching a staggering 828 million people [8]. An effective method to boost the nutritional content of food involves food fortification, which entails the addition of essential minerals and vitamins [9]. This fortification process can occur either on an industrial scale [10] or at the consumer's table [11]. Factors such as targeting foods that are economically feasible, readily accessible, and commonly consumed in large quantities in a particular region are one of the strategies for implementing industrial fortification [2].

1.1. Biofortification: Technique of Nutrient Enhancement

Biofortification is a strategy aimed at elevating the nutritional quality of food by increasing levels of essential vitamins and minerals in their edible parts [12,13]. This agricultural approach is designed to address deficiencies, such as "hidden hunger", which affects millions of people worldwide. Biofortification involves breeding crops through conventional or biotechnological methods to elevate the concentration of key nutrients, such as iron, zinc, vitamin A (Retinol), and others, in staple foods like rice, wheat, maize, and beans. By integrating this approach into agricultural practices, biofortification offers a sustainable and cost-effective solution to improve the nutritional status of populations, particularly in regions where access to diverse and nutrient-rich diets is limited. The goal of biofortification is to combat malnutrition and contribute to global efforts to achieve nutritional security and promote public health [7].

However, the addition of micronutrients to food through fortification has the potential to alter its quality, shelf life, color, flavor, and texture, thereby potentially resulting in a diminished level of acceptance by consumers [14,15]. Despite being a more cost-effective method compared with the use of pharmaceutical supplements, it remains economically challenging for populations grappling with micronutrient malnutrition [16]. The study is based on the different approaches of biofortification applied to a specific crop plant potato to enhance its nutrient quality along with specific desired nutrient values. However, the selection of potatoes for this study is backed with concrete validations. Potato stands as an ideal candidate for biofortification initiatives. With a history of contributing to the human diet for millennia, potato tubers remain a fundamental staple, crucial for global food security. Beyond providing substantial energy, potatoes are rich in compounds possessing nutraceutical properties, encompassing minerals, vitamins, proteins, and specialized metabolites like glycoalkaloids and phenolics [17].

1.2. Potato as the Most Suitable Crop Selected for Biofortification

Potatoes stand out as a versatile and nutritionally rich crop, offering a significant opportunity to address micronutrient malnutrition [18]. Widely cultivated across various climatic conditions, including temperate, tropical, and even subtropical regions, potatoes have become a staple in many countries due to the easy method of cultivation, low expenses, and high nutrient values, along with higher yield per unit area in minimal time consumption [19]. This tuberous crop is not only consumed as a fresh vegetable but also has a substantial industrial demand as processed food. Recognized for its nutritional value, potatoes serve as a cost-effective source of carbohydrates, proteins, minerals, vitamins, and dietary fibers. The nutrient parameters of potatoes have been depicted in Table 1. Notably, they provide substantial quantities of essential nutrients, such as vitamin C (Ascorbic acid), vitamin B6 (Pyridoxine), vitamin K (phylloquinone), iron, and folate [20,21]. While the nutrient composition may vary slightly among potato varieties, colored potatoes, in particular, emerge as rich sources of various antioxidants like polyphenols, anthocyanins, carotenoids, and flavonoids [22,23], contributing to their appeal as a health-promoting food choice, even after cooking [24–26].

Table 1. Nutrient values of potatoes.

SL No	Name of Parameter	Values/100 gm	SL No	Name of Parameter	Values/100 gm
1	Protein	2.57 g	8	Potassium	411 mg
2	Energy	59 kcal	9	Iron	3.14 mg
3	Total dietary fibre	2.1 g	10	Calcium	30 mg
4	Vitamin C	10.9 mg	11	Sodium	12 mg
5	Vitamin B 6	0.237 mg	12	Zinc	0.32 mg
6	Riboflavin	0.038 mg	13	Thiamin	0.02 mg
7	Folate	17 µg	14	Niacin	1.03 mg

Similarly, if we validate the boiled potatoes (cooked ones), the nutrient content would also vary [27], as provided in Table 2.

Table 2. Nutrient values of boiled potatoes.

Name of Parameter	Values/100 gm	Name of Parameter	Values/100 gm
Protein	2.11 g	Vitamin A	3.8 IU
Carbohydrate	25 g	Vitamin C	9.5 mg
Energy	107 kcal	Vitamin K	2.6 mcg
Total lipid	0.15 g	Vitamin E	0.01 mg
Sugar	1.1 g	Riboflavin	0.02 mg
Total dietary fat	2.3 g	Niacin	1.6 mg
Carotene	2.5 mcg	Thiamin	0.1 mg
Pantothenic acid	0.67 mg	Folate	11.3 mcg
Lutein & Zeaxanthin	11.3 mcg	Calcium	10 mg

Potatoes possess substantial nutritional value, which is attributed to numerous essential phytochemicals that offer better health advantages [28]. Key constituents of potatoes include various phytonutrients, along with essential mineral elements, as well as vitamins [29]. Due to several nutrient benefits, it is mostly used as a fundamental staple food and is crucial for global food security. Hence, nutrient enhancement in such a crop would be pivotal. The current study is a systematic compilation of different approaches available for the biofortification of potatoes for the enhancement of their nutritional availability, along with enhancing their tuber size for maximum yield. The concerned study focuses mostly on the three basic available approaches to biofortification, with specific references to modern techniques in this field.

2. Methodology

The current literature review adopted the systemic review method to analyze the available biotechnological innovations that can be used for nutrient enhancement in the case of potatoes. The review was initiated by searching three databases, namely SCOPUS, PubMed, and ScienceDirect, in order to gather articles using relevant keywords, like "biofortification of potato", "biofortification", "nutrient enhancement in potato", "biotechnological innovations", "biotechnological innovations for biofortification", "biotechnological innovations for biofortification of potato", etc. The selection of a theme for the review was conducted after a stringent analysis of the research papers retrieved under the aforementioned keywords. Papers supporting various results in the concerned field were obtained for the critical conceptualization of the extracted data, and it took at least 3–4 months for the screening. The analysis was conducted using a research framework that focuses on the title screening of these papers under various research themes. To prevent bias in theselection of papers, the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow chart was then prepared, demarcating the inclusion and exclusion criteria. Inclusion parameters included papers with prominent experimental results according to the requirement of the selected theme and papers pertaining to selected major and minor themes, while exclusion parameters included duplicates, publications before 2000, and conference papers. The ScienceDirect database was used to obtain several bibliometric data to analyze various perspectives of the study contributions for the same research topic.

3. Result

Potatoes, being a low-calorie food source, contain protein with a biological value equivalent to 75% of egg and milk protein, and they are also abundant in minerals and vitamins [30]. Given the global challenges of a growing population and diminishing resources, potatoes possess significant potential to complement traditional cereal crops. In the context of this, India holds the position of the world's second-largest producer of potatoes, trailing only behind the Republic of China [31]. India's potato production, approximately 45 million metric tons, constitutes around 7.75% of the world's total output and continues to rise due to an expanding cultivated area (Figure 1) [32]. The versatility and nutritional value of potatoes make them a promising resource in addressing the increasing demand for food in a world with limited resources [33].

In the last ten years, many researchers have been working continuously on this aspect to obtain a clear idea regarding the mechanism of biofortification for different vegetables, especially potatoes. The bibliometric analysis depicts the total publication of papers on the biofortification of potatoes in the ScienceDirect database (Figure 2).

Database searches could retrieve a total of 6562 research papers using the aforementioned keyboards. After the removal of duplicates and papers published before 2000, approximately 5593 were found to fit into the core theme (biotechnological innovations for the biofortification of potatoes) and thus were finally subjected to quality screening. The quality screening considered parameters like relevance to the theme, the aim of the study, the methodology applied, and the results obtained. The papers excelling in all these parameters were taken forward for extensive analysis. Through this process, the 45 most suited papers were finally chosen for data extraction. The PRISMA for the current review depicts selection criteria, including the exclusion and inclusion parameters of the current review (Figure 3). After screening the brief abstracts, 433 were selected for full-text screening through critical appraisal.

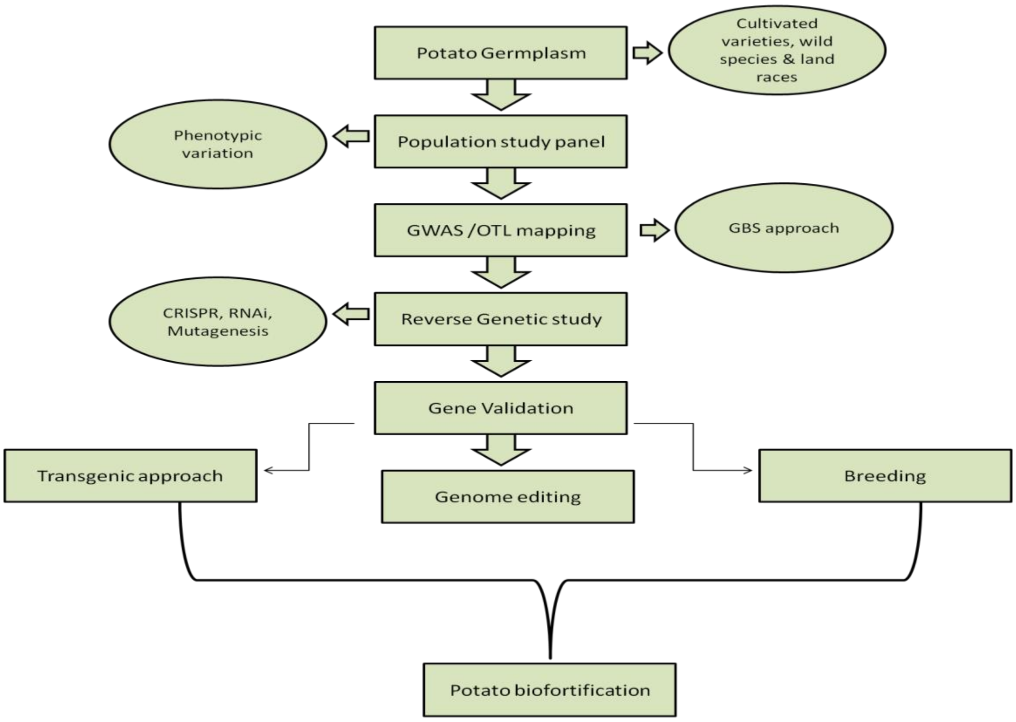

Figure 1. Flow chart suggesting possible ways available for potato fortification for nutrient enrichment.

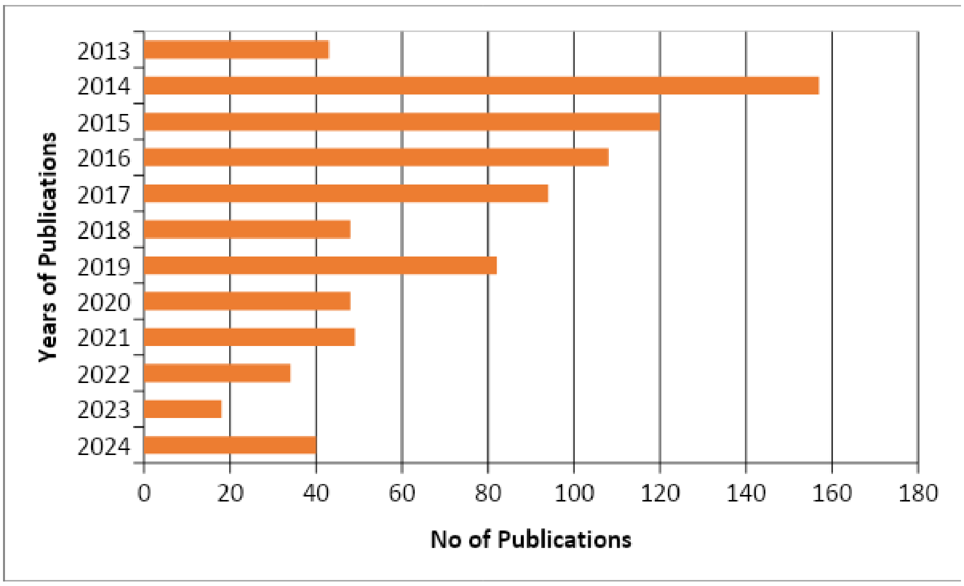

Figure 2. Papers published under "biotechnological innovations for biofortification of potato" (ScienceDirect database).

For the data extraction the key data the selected papers were screened and analysed on the following set of particulars: details of the authors with year of publication, biofortification strategies, improved nutrient value, and outcome. These key data sets are summarized in the following table (Table 3).

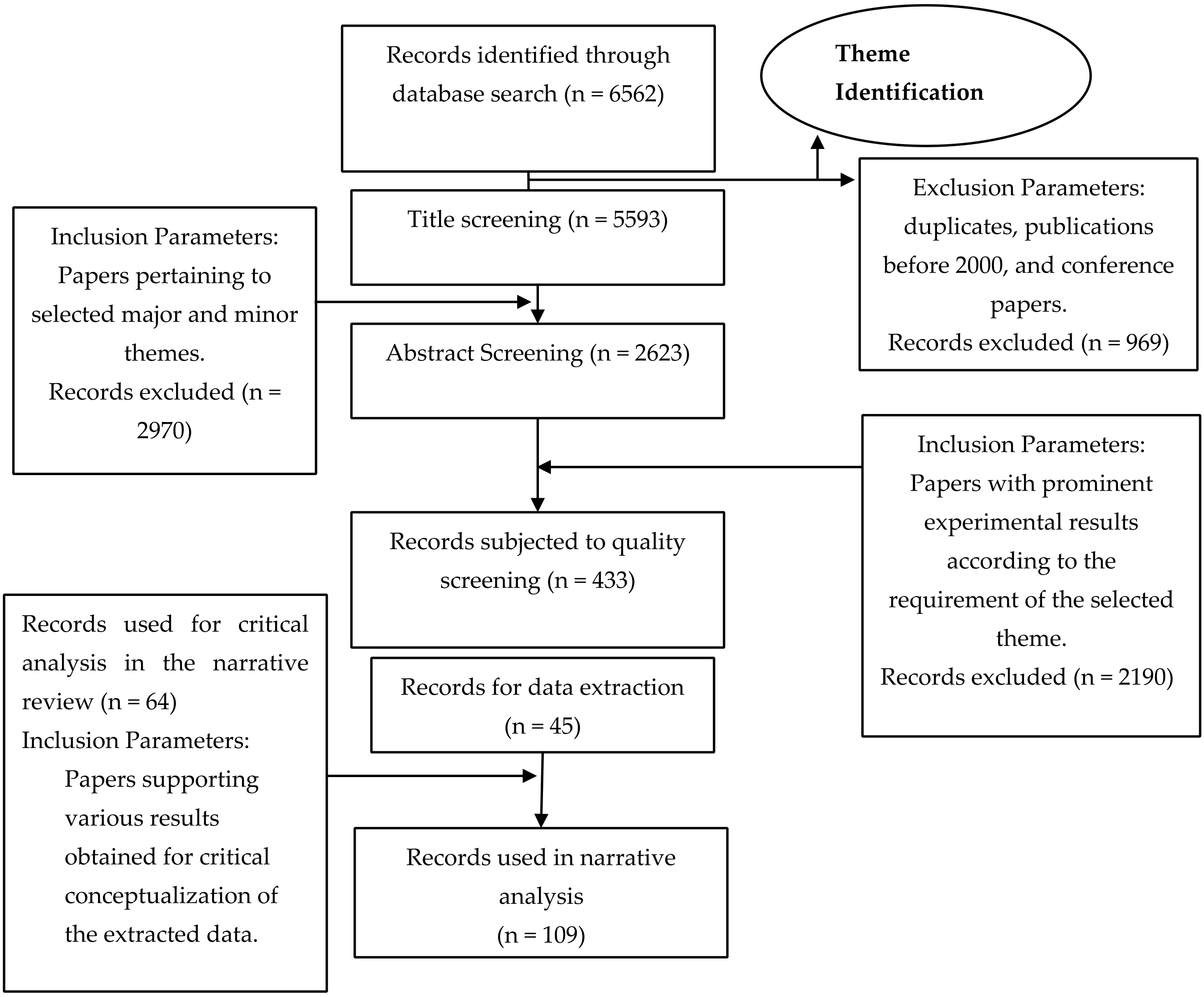

Figure 3. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) scheme for the selection of articles for the systematic review.

Table 3. Data extraction for the quality papers selected for review under the identified themes.

Sl No	Name of Authors with Year	Biofortification Strategies	Improved Nutrient Value	Outcome
1	[34]	"Antisense inhibition of threonine synthase"	Increasing methionine content (239-fold higher	Higher nutrient content
2	[35]	"Zeaxanthin epoxidase gene expressions in transgenic mode"	Zeaxanthin content	Higher zeaxanthin content
3	[36]	Incorporating *PSY* gene	Provitamin A and lutein	Higher nutrient content
4	[37]	"Expression of the *Arabidopsis* H^+/Ca^{2+} transporter scax1"	Calcium content	Higher calcium content
5	[38]	"Expression of an *Arabidopsis* CAX2 variant"	Increases calcium levels	Higher calcium content

Table 3. *Cont.*

Sl No	Name of Authors with Year	Biofortification Strategies	Improved Nutrient Value	Outcome
6	[39]	"Simultaneous incorporation of *PSY*, phytoene desaturase, and lycopene β-cyclase genes"	Carotenoids	Higher nutrient content
7	[39]	"Tuber-specific silencing of lycopene epsilon cyclise"	Carotenoid content	Higher carotenoid content
8	[40]	Transgenic approach of *Orange* (*Or*) gene from cauliflower in potato	B-carotene accumulation	Higher β-carotene accumulation
9	[41]	Transgenic approach for *cysE* gene	cysteine and glutathione contents	Higher cysteine and glutathione contents
10	[42]	"RNAi silencing of beta-carotene hydroxylase gene"	Beta-carotene content	Higher Beta-carotene content
11	[43]	Incorporation of orange cauliflower mutant *Or* gene	Carotenoids, phytoene, phytofluene, and z-carotene content	Higher nutrient content
12	[44]	"Co-expression of cystathionine γ-synthase (*CgS*Δ_{90}) and methionine-rich storage protein"	Methionine content	Higher methionine content
13	[45]	"Overexpression of strawberry *GalUR*"	Vitamin C content	Higher vitamin C content
14	[46]	Transgenic approach	ascorbic acid content	Higher ascorbic acid content
15	[46]	"Over-expression of L-gulono-γ-lactone oxidase gene"	L-Ascorbic acid content	Increases ability to withstand abiotic stresses
16	[47]	"Overexpression of two dehydroascorbate reductase genes"	Ascorbic acid contents	Higher Ascorbic acid content
17	[48]	"Overexpression of D-galacturonic acid reductase"		Tolerance in transgenic potato to abiotic stress
18	[49]	RNAi silencing of *SSIII* gene	phosphorus and starch content	Higher phosphorus and starch content
19	[50]	Transgenic approach for *PsGPT* gene	starch yield	Higher starch yield
20	[51]	Expression of prleg polypeptide potato	Methionine content	Higher Methionine content
21	[52]	Over expression of dihydroflavonol reductase	Phenolic antioxidant content	Transgenic potato with efficient nutrient values
22	[53]	Silencing of *stmgl1*	Higher methionine to isoleucine ratio	Higher methionine to isoleucine content
23	[54]	Genome-wide association studies	Starch of the amylopectin	Enhancing its industrial application
24	[55]	Expression of auxin synthesis gene tms1	in vitrotuberization	Higher tuber yield
25	[56]	"Overexpression of the sweet potato ibor gene"	Carotenoid content	Elevates tolerance to environmental stresses
26	[57]	TALEN genes *GBSS* for genome editing	Starch quality	Better Starch quality
27	[58]	Expression of lycopene β-cyclase [*stlcyb*]	Beta-carotene content	Higher Beta-carotene content

Table 3. *Cont.*

Sl No	Name of Authors with Year	Biofortification Strategies	Improved Nutrient Value	Outcome
28	[59]	"Over expression of *AtCYP21-4* and *OsCYP21-4* genes"	Mannosidic-glycoproteins content	20% increase in mannosidic-glycoproteins
29	[60]	Agronomic biofortification	iron and zinc Content	Higher iron and zinc content
30	[61]	"Transient expression of transcription activator-like effector nucleases (TALEN) Genome editing of *StvacINV2*"	cold-induced sweetening (CIS) or reducing sugar content	Regulation of CIS
31	[62]	Integrated metabolic engineering strategy	Oil content	Higher oil content
32	[63]	"Overexpression of cystathionine γ-synthase and silencing of endogenous methionine γ-Lyase"	Methionine content	Higher methionine content
33	[64]	"Multiallelic mutagenesis in tetraploid potato through CRISPR-Cas9 expression at *GBSS* gene"	Starch quality	Better Starch quality
34	[65]	"Transgenic approach with Single nucleotide polymorphism markers"	Folate content	High folate content
35	[66]	"Overexpression of PDX-II gene"	"Vitamin B6 content"	Higher vitamin B6 content
36	[20]	"Tuber-specific expression of four folate biosynthesis genes *HPPK/DHPS* and/or *FPGS* in mitochondrial folate biosynthesis"	Folate biofortification	"Augmentation of folates to satisfactory levels (12-fold) with stability"
37	[67]	"Agronomic biofortification (Tuber priming)"	zinc Content	Higher zinc content
38	[68]	Agronomic biofortification (foliar application)	Selenium Content	Higher Selenium content
39	[69]	Agronomic biofortification (titanium foliar application)	Fe, Zn, Mn, Ti content	Higher nutrient content
40	[70]	"Inhibition of cysteine StPI 143 and StPI 146"	reduction in protease activities	Regulate free amino acid contents
41	[71]	"Wrinkled1, Diacylglycerol acyl transferase 1 and oleosin"	"30-fold increase in triacylglycerols"	Higher triacylglycerols content
42	[72]	"Application of foliar microelement-containing solutions"	"Enhanced micronutrients content (B, Cu, Fe, Mn, Mo and Zn)"	Fortified micronutrients content
43	[12]	"Foliar spraying with KIO_3 in a dose of 2.0 kg I ha^{-1}".	Iodine content	"Potatoes biofortified with iodine can be a source of i in a daily diet"
44	[73]	"Using irrigationWater containing iodine at concentrations of 0.1 and 0.5 mg/L"	Iodine content	Higher iodine content
45	[26]	"Marker-assisted selection, speed breeding and transgenic approaches"	Iron content	Higher iron content

4. Discussion

Biofortification aims to boost the levels of essential micronutrients in the consumable parts of crop plants, targeting objectives such as increased mineral and vitamin content, elevated essential amino acids, improved fatty acid composition, and heightened antioxidant levels [74]. This approach not only ensures an ample supply of calories to meet energy requirements but also delivers all the vital nutrients essential for overall health. Additionally, by focusing on biofortifying crops commonly consumed by economically disadvantaged populations worldwide, this strategy holds the potential to substantially enhance the nutritional intake of these vulnerable communities [75,76].

Potato biofortification involves enhancing the nutritional content of potatoes, particularly in terms of essential vitamins and minerals. Several approaches are employed to achieve this goal. However, the conventional breeding approach, agronomic biofortification, transgenic approach, CRISPER technology, and reverse genetic approaches such as Association mapping and the quantitative trait loci (QTL) method are found to be effective in enhancing the nutrient content in potatoes [26,77,78].

4.1. Conventional Breeding

Conventional breeding stands as the most widely accepted approach to biofortification, providing a sustainable and cost-effective alternative to both transgenic and agronomic strategies. The feasibility of conventional breeding relies on having ample genotypic variation in the targeted trait. Breeding programs leverage this diversity to enhance the mineral and vitamin levels in crops such as potatoes [79]. In this process, parent lines exhibiting high nutrient content are systematically crossed with recipient lines possessing desirable agronomic traits over multiple generations, resulting in plants with the desired combination of nutrient and agronomic characteristics. However, the success of breeding strategies can be constrained by the limited genetic variation within the gene pool. Overcoming this limitation may involve crossing with distant relatives to gradually introduce the desired trait into commercial cultivars. Alternatively, new traits can be directly introduced into commercial varieties through mutagenesis [77]. The International Potato Center (CIP) and Harvest Plus collaborated to create advanced breeding material with heightened iron and zinc content. This involved crossing diploid Andean landrace potatoes, rich in zinc and iron, with disease-resistant tetraploid clones [2,80]. The CIP Potato Biofortification with a baseline of 0.48 mg/100 g FW of iron and 0.35 mg/100 g FW of zinc elevated to 0.73 mg iron and 0.63 mg zinc/100 g FW after three cycles of breeding [2]. Traditional breeding methods are used to develop potato varieties with improved nutritional profiles. This involves selecting and crossing potato plants with desirable traits, such as higher levels of specific nutrients, like iron, zinc, or vitamins. Through successive generations, breeders aim to stabilize and enhance these traits in the resulting potato varieties [2]. In 2012, researchers explored genetic diversity linked to micronutrient concentrations across 18 potato clones, uncovering notable variations in the concentrations of iron, zinc, copper, and manganese in potatoes. Additionally, Ref. [81] observed extensive nutritional diversity, encompassing dry matter, protein, as well as iron and zinc content.

4.2. Agronomic Practices

Agronomic biofortification is a strategy employed in agriculture to enhance the nutritional content of food crops, specifically focusing on increasing the concentrations of essential micronutrients in the edible portions [80,82]. This approach involves two key practices: seed tuber priming and the application of mineral fertilizers. Seed tuber priming refers to treating the seeds with specific nutrient solutions before planting [77], aiming to enhance the uptake and accumulation of micronutrients in the growing plants. Additionally, mineral fertilizers containing essential micronutrients can be applied to crops either through foliar spraying or soil application, contributing to the overall nutrient enrichment of the plants. Agronomical biofortification addresses nutritional deficiencies in staple crops, promoting healthier diets and combating malnutrition on a broader scale [80,83].

"Agronomical biofortification involves the process of seed tuber priming and the utilization of mineral fertilizers to augment the concentrations of micronutrients in the edible parts of food crops" [83]. In a study by [67], successful zinc biofortification in potatoes was achieved by priming the tubers with a 10 mg/mL Zn solution for a duration of 12 h.

The application of micronutrient-containing mineral fertilizers to plants can be carried out either through foliar or soil application methods [84,85]. Agronomic biofortification, though it is straightforward and cost-effective, demands careful consideration regarding the nutrient source, application technique, and environmental impact. Consistent application is required in each crop season, making it less economically efficient in certain situations [26].

The effectiveness of agronomic biofortification is contingent on several factors, including soil composition, pH levels, mineral mobility, accumulation, environmental conditions, and the developmental stage of plant growth during fertilizer application [80]. However, as a method to enhance the bioavailability of nutrients synthesized through plant metabolism, it proves to be less efficient. Specifically, for iron (Fe), this approach faces limitations since Fe in soil is immobilized in the ferric form, whereas plants absorb Fe in the ferrous form, making the process less effective [86]. Furthermore, agronomic biofortification is a temporary and costly means of enhancing nutrient content, requiring the repetitive implementation of the same agronomic practices.

4.3. Molecular Approach

4.3.1. Transgenic Cultivars

The transgenic approach for potato fortification involves the genetic modification of potato plants to enhance specific nutritional attributes, such as increased levels of essential vitamins, minerals, or proteins. This is achieved by introducing foreign genes into the potato genome, often derived from other organisms, to confer desired traits. In the context of fortification, these traits may include elevated concentrations of nutrients that are essential for human health, such as increased levels of vitamins or minerals [77,87]. Advances in biotechnology enable the use of molecular techniques to directly manipulate the genetic material of potatoes. This includes techniques like marker-assisted selection, where specific genetic markers associated with desired traits, such as high iron content, are identified and used to guide the breeding process. Genetic engineering may also be employed to introduce or enhance specific genes responsible for nutrient accumulation [88–90].

In genetically modified potatoes, the augmented protein is located within the cytoplasm or vacuole. The tubers of seven genetically engineered potato varieties demonstrated a protein increase of up to 60% compared with control counterparts [87]. Alongside the heightened protein content, the transgenic potatoes exhibited an enhanced photosynthesis rate, ultimately resulting in increased total biomass and plant yield. Notably, the transgenic potato cultivar Desirée also showcased a significant rise in methionine content, an essential amino acid crucial for multiple cellular pathways [63]. Using RNAi technology, the overexpression of an exogenous gene, *Arabidopsis thaliana* cystathionine γ-synthase (AtCGS), coupled with the suppression of the host gene *S. tuberosum* methionine γ-lyase (StMGL), led to almost a two-fold concentration of free methionine in the transgenic tubers compared with controls [63]. Importantly, experimental studies on engineered plants revealed no discernible differences in morphology or yield when compared to control plants. Other attempts to increase protein content in potatoes through various studies encountered limited success and posed yield penalties [44,91,92]. Taedong Valley, a modified potato variety, was developed by introducing the GLOase gene, derived from rat cells and responsible for L-gulono-γ-lactone oxidase expression. This genetic modification resulted in a substantial increase (141%) in the content of L-ascorbic acid, vitamin C [46,77].

Some of the genetically modified potato varieties include Lugovskoi Plus, Amflora™, NewLeaf™ Y, etc. The European company BASF™ developed Amflora™ potatoes, which only contain amylopectin through *GBSSI* down-regulation that reduces amylase development. Similarly, NewLeaf™ Y, developed by *Cry3A* and PVY coat protein introduction for Colorado potato beetle and potato virus Y resistance by J.R. Simplot ® company [93]. Furthermore, tissue-specific transgenesis for biofortification by [20] can increase the concentrations of micronutrients in the edible portion of the targeted crop. For instance, the introduction of the PDXII gene from *Arabidopsis thaliana* into potatoes, driven by the CaMV35S promoter, resulted in increased accumulation of vitamin B6 and improved tolerance to abiotic stress induced by methyl viologen and salinity [66]. Similarly, the incorporation of *Arabidopsis* ABF4 in potatoes demonstrated enhancements in tuber yield, quality, and tolerance to abiotic stress like salinity and drought tolerance [94]. A genetically modified potato exhibiting increased levels of methionine and cysteine amino acids was achieved by introducing specific genes responsible for cysteine and methionine metabolism. This approach was adopted due to the distinct biosynthetic regulation of these amino acids in potatoes, as opposed to findings in other plants like *Arabidopsis* [95]. In potato tubers, the enhancement of the provitamin A has been achieved through the introduction of the *PSY* gene [36], as well as through the incorporation of PSY, phytoene desaturase, and lycopene β-cyclase genes [39]. In a study by [70], the enhanced expression of protease inhibitors, specifically cysteine StPI 143 and StPI 146, in potatoes led to a reduction in protease activities. This genetic modification resulted in decreased levels of tyrosine, as well as a decline in the overall content of total free amino acids. In a different investigation, a genetically modified potato that expressed elevated levels of *AtCYP21-4* and *OsCYP21-4*, specifically a cyclophilin protein, exhibited a notable rise of about 20% in mannosidic-glycoproteins. This genetic modification also correlated with a substantial increase in both the number and weight of tubers [59].

4.3.2. Marker-Assisted Selection

Association Mapping and Quantitative Trait Loci (QTL)

Association mapping and quantitative trait loci (QTL) analysis are two genetic approaches used in fortification programs to identify and understand the genetic factors influencing the levels of specific nutrients or compounds in crops [78]. The first one, Association mapping, also known as genome-wide association study (GWAS), involves studying the association between genetic variations (typically single nucleotide polymorphisms, or SNPs) and specific traits or characteristics. On the other hand, the second one, quantitative trait loci (QTL) analysis, involves identifying and mapping regions of the genome that are associated with the variation of quantitative traits, such as nutrient content, yield, or disease resistance [77]. Through these techniques, possible genes, markers, and quantitative trait loci (QTL) linked to micronutrient content have the potential to be recognized (Figure 4). Essential for comprehending the genetic distinctions among breeding clones, progeny crosses, and wild species, pivotal breeding tools include QTL analysis, whole-genome sequencing, and the identification of associations between markers and traits [96,97].

The protein content stands as a significant quality trait in the potato industry. Through genetic mapping analysis, potential quantitative trait loci (QTL) were identified on chromosomes 2, 3, 5, and 9. Subsequent cofactor QTL analyses unveiled two concealed QTL on chromosomes 1 and 5 [98]. In the case of starch content, on average, a minimum of 12 QTL for tuber starch have been identified [99], with two documented QTL for the size of starch granules: SGS02-8 and SGS03-8 on chromosome VIII [100]. Furthermore, the characteristics and makeup of storage starch vary from those of leaf starch [101].

4.3.3. Genomic Editing

Transcription Activator-Like Effector Nucleases (TALENs)

TALENs are a type of engineered nuclease used in genetic engineering and genome editing. They are designed to target and modify specific DNA sequences in an organism's genome. TALENs were developed as a result of combining two main components: transcription activator-like effectors (TALEs) and a nuclease [57,61]. The acetolactate synthesis (*ALS*) gene, responsible for encoding acetohydroxy acid synthase and initiating the synthesis of branched amino acids, is susceptible to certain herbicides, like imazamox in the case of potatoes [102]. Using the TALEN system, the mutated *ALS* gene was effectively employed for the precise integration of foreign genes into the potato host [103]. Starch modifications were achieved by [57] through the development of the "Emerald-Gateway TALEN system", a distinctive delivery system that targets the granule-bound starch synthase (*GBSS*) gene in the host for site-specific mutations. This gene plays a crucial role in starch biosynthesis, impacting starch quality during granulation.

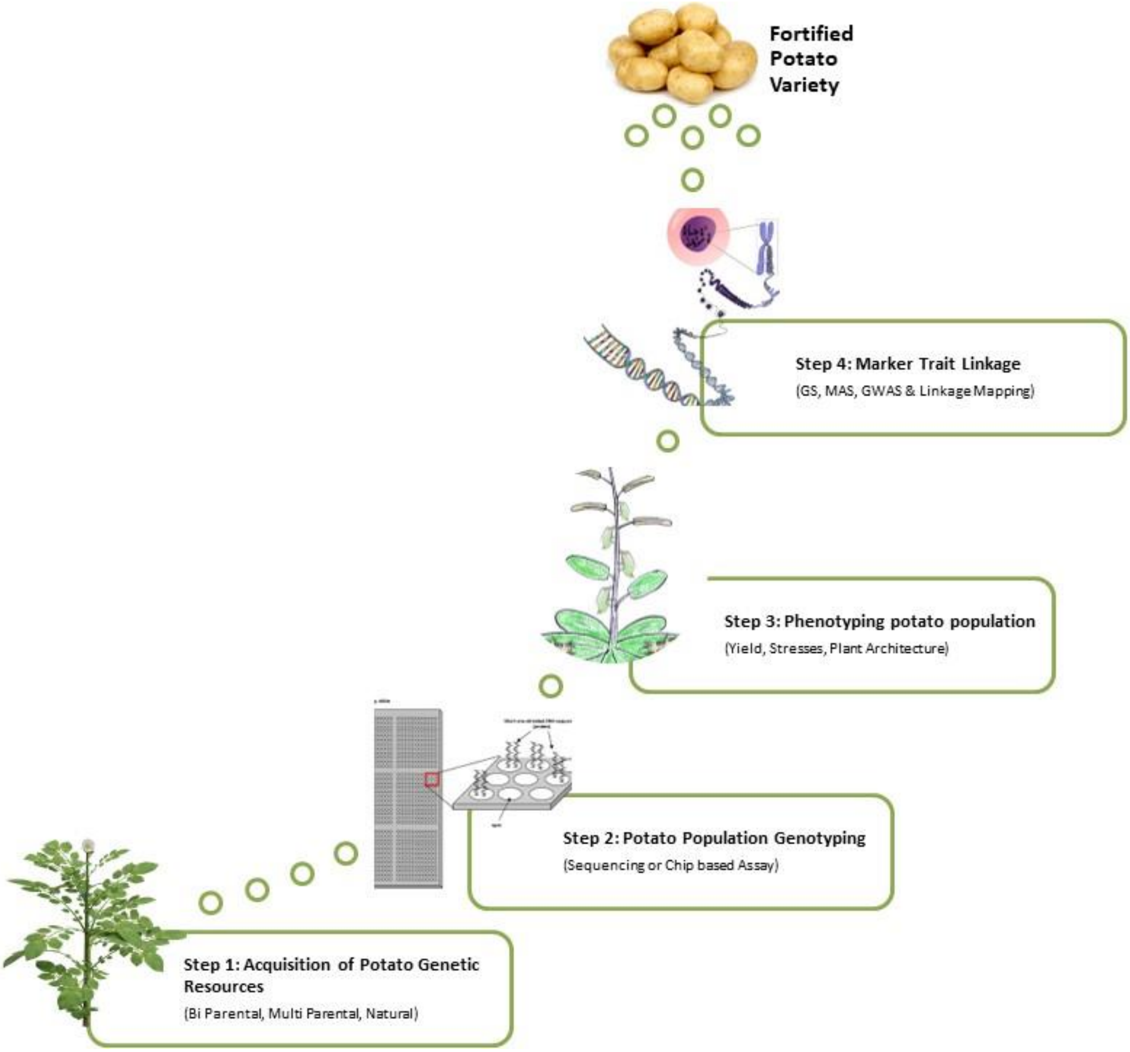

Figure 4. Genome-assisted breeding.

CRISPR-Cas Genome Editing Method

CRISPR-Cas (Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated proteins) is a revolutionary genome editing method that allows for the precise modification of DNA within an organism's genome. CRISPR-Cas has revolutionized genetic research and biotechnology due to its simplicity, versatility, and efficiency. It has applications in a wide range of fields, including gene therapy, agriculture, and functional genomics [64,104].

The CRISPR-Cas9 technique has been effectively employed in potatoes using geminivirus replicons (GVRs) [104,105]. Given that potatoes respond well to plant tissue culture-based propagation, as highlighted by [106], it becomes relatively straightforward to cultivate nutrient-rich, superior, non-genetically modified (non-GMO) potato plants using these strategies for future applications. These methods present a viable substitute for transgenic approaches, as they eliminate the need for permanently inserting foreign genes.

Biotechnological breeding tools offer significant benefits in fortifying potatoes with desirable traits, such as enhanced nutritional content and disease resistance. Research, such as that by [70,78], highlights the potential of biotechnological approaches like marker-assisted selection, CRISPR-Cas9 technique, transgenic approach, and agronomic biofortification to expedite the breeding process, leading to the development of nutrient-rich potato varieties with improved agronomic traits. However, these methods are not without restrictions; concerns regarding public acceptance, regulatory frameworks, and potential environmental impacts necessitate thorough risk assessment and communication strategies, as emphasized by [89]. Adherence to rigorous safety protocols and transparent communication channels are crucial to ensure the successful integration of biotechnological tools in potato breeding programs, addressing both societal needs and regulatory requirements.

4.4. Future Prospective

The introduction of transgenic biofortified products, particularly in the case of potatoes intended for human consumption, may encounter potential regulatory and social rejections. Regulatory bodies often impose stringent assessments to ensure the safety of genetically modified products in food, which could lead to delays or even the rejection of these products entering the market. Concerns about the long-term health effects, environmental impacts, and unintended consequences of genetic modification may contribute to regulatory hurdles. Moreover, social acceptance of genetically modified products varies widely, with segments of the population expressing skepticism or outright opposition to their consumption due to perceived risks and ethical considerations related to altering the genetic makeup of food. Addressing these concerns through transparent communication, robust risk assessment, and engagement with stakeholders is crucial to navigating regulatory processes and fostering the public acceptance of transgenic biofortified products, like genetically modified potatoes, for human consumption [80].

5. Conclusions

While various approaches are available, biofortification emerges as a highly sustainable method to deal with food scarcity and related issues. Dietary diversification, pharmaceutical supplementation, and food fortification, while effective, pose affordability challenges for the economically disadvantaged. In comparison, crop biofortification proves to be a more sustainable alternative. Potato crops respond significantly to agronomic practices like tuber priming and the application of soil and foliar fertilizers, necessitating farmers' awareness of the optimal dosage and timing for maximizing benefits. Understanding the genetic basis of micronutrient concentrations in potato tubers can facilitate biofortification efforts. Although traditional breeding experiments are time-consuming, advances in biotechnological tools enable the design of more precise and accurate breeding programs to enhance micronutrient concentration in potatoes.

Research dedicated to food safety and security presents significant avenues to address the growing demand for food, particularly in countries facing food deficits. The rapid advancements in plant genetic engineering offer innovative tools to develop crops with improved yield and nutritional characteristics. In this context, the potato crop holds substantial potential to contribute to food security by providing cost-effective, high-energy food on a sustainable basis. Numerous studies have showcased the incorporation of nutritional traits in potatoes. To address these regulatory challenges, research on New Breeding Techniques (NBTs) should now prioritize the generation of transgene-free products, especially for food crops. Given that the process of transgene removal through segregation is time-consuming in vegetatively propagated crops like potatoes, the use of agroinfiltration and protoplast transformation for delivering NBTs' reagents presents a rational approach for transgene-free potato production.

Author Contributions: S.A.: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Visualization, Writing—original draft; A.K.: Software, Investigation, Data curation, Writing—review and editing. A.T.: Validation, Resources, Funding acquisition, Writing—review and editing. Y.G.: Writing—review and editing, Validation, Supervision, Funding acquisition, Conceptualization, Supervision, Writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

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