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Review

Intercropping Systems to Modify Bioactive Compounds and Nutrient Profiles in Plants, Do We Have Enough Information to Take It as a Strategy to Improve Food Quality? A Review

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Abstract: Various environmental, food security and population health problems seem to be related to intensive agriculture production worldwide. This type of food production system impacted the loss of biodiversity and natural habitats; high usage rates of agrochemicals and natural resources had affected soil composition, human health, and nutritional plant quality in rural areas. Intercropping agroecological systems that respect agrobiodiversity could significantly benefit ecosystems, human health, and food security by modifying the nutritional profile and the content of some health-promoting bioactive compounds of the species cultivated in this system. Research on intercropping strategies focuses on the benefits they can offer to ecosystems and less on nutrient plant composition, leaving information scattered when this theme should be more studied due to the critical impact it could provide for human nutrition. Therefore, this review aims to collect viable details on the investigation status of nutrients and bioactive compounds profile in intercropping systems by verifying different regions of the world with unique mixed crops using plant species, along with the criteria for combining them, as well as the nutrients and bioactive compounds analyzed to show what intercropping systems can contribute to food availability and quality.

Keywords: food production; sustainable agriculture; human health; nutrients; bioactive compounds

1. Introduction

The world population growth and lifestyle changes have increased worldwide food demand [1,2]. Intensive food production systems like monocultures have been implemented to satisfy this demand. Moreover, intensive agriculture has hurt the environment, such as the loss of biodiversity and natural habitats and excessive use of agrochemicals and fertilizers, which leads to the loss of fertile soils by damaging the soil microbiota (plant-soil interaction) [3,4] and contamination of aquifers affects the availability of nutrients required by crops [5,6,7]. Furthermore, intensive agriculture systems have yet to be able to eradicate hunger in developing countries; even worse, the set of these faulty agricultural practices causes products obtained for human and animal consumption to be of low nutritional quality, which could be related to health issues [8]. Thus, various food production strategies must be tested to guarantee adequate food supply. It has been stipulated that balancing biodiversity conservation and food security is the key to global sustainable development [3,9]. In this context, sustainable agriculture integrates different areas by taking care of the environment, the market, policy, research and innovation, and several societal perspectives [10], like improving people's health status [11], through food quality improvement [12]. Therefore, food included in sustainable agriculture must be accessible, affordable, safe, and equitable, which also complies with the dimensions of food security [13, 14].

Intercropping systems, which are traditional farming practices, could be an alternative to sustainable production systems [15]. The characteristics of these cultivars are to achieve an interaction that benefits the different species involved and provides more regulation services to ecosystems [16, 17]. Intercropping systems could have a positive impact on the environment and society. They prevent soil erosion and improve soil fertility by enriching soil microbiota. Moreover, they can increase biodiversity and conservation of natural habitats due to the different families of plants found within the same area and the natural habitat of many endemic species. Naturally regulating pests, diseases, and weeds could considerably reduce the use of fertilizers and agrochemicals [17].

Furthermore, they can offer farmers the opportunity to obtain socioeconomic benefits and food security since multi-cropping can increase yield [18], which allows them to have more available food or a more significant sale of products [19, 20, 21]. All these characteristics have been widely studied over the years; nevertheless, just a few studies about the changes in the quantity and quality of nutrients and phytochemicals that benefit human health due to the interaction of the species involved in intercropping have been carried out. An example is the amount of soluble and insoluble fiber, increased phenols and flavonoids, amino acids, and other phytochemicals found in finish products and/or their flowers [9, 22, 23]. The study of these possible changes is relevant for food and nutritional security since, for developing countries, intercropping systems could provide a large part of family nutritional needs [14].

To our knowledge, a study has yet to be conducted that compiles the research carried out in intercrops to find changes in the quantity and quality of bioactive compounds beneficial to human health or macronutrients. Therefore, the objective of this review is to recollect viable information about the actual investigation status of the regions of the world where intercropping systems are being implemented for nutritional improvement purposes, the species that have been used in these crops, and the criteria for combining these species, as well as the nutrients analyzed.

2. Food security by intercropping systems

In recent years, there has been greater awareness of the challenges and actions to be taken to eliminate hunger and malnutrition worldwide, including food systems management. In this sense, agriculture plays a vital role in most developing countries. However, due to population growth, industrial development, and different political systems, more than current food systems are needed to feed this growing population [2]. Although they implemented intensive food production systems, the goal of eradicating world hunger has yet to be achieved [24]. Indeed, around the world, approximately 2.370 million people experienced food insecurity at a moderate or severe level in 2020 [25].

Food security is a term that was first introduced in 1970, and numerous modifications have been made to its definition to adapt it to the current population's worldwide needs [26]. All existing reports generally agree that food security is where a sustained food supply is received [27]. The World Food Summit added that food security focuses on four main dimensions: availability, accessibility, utilization, and stability. These four dimensions do not necessarily coincide. For this reason, food security cannot be adequately measured with a single indicator. A multidimensional analysis can be a valuable tool to assess and compare various food security indices at the regional and national levels [28].

In this sense, in the '90s, the most popular definition emitted by the Food and Agriculture Organization (FAO) defines food security as "a situation that exists when all people, at all times, have physical, social and economic access to sufficient, safe and nutritious food that meets their dietary needs and food preferences for an active and healthy life" [29]. It was the first time that emphasis was placed on the importance of nutrient quality contained in foods for human consumption, giving it a place to dimension Utilization [26]. Moreover, it is known that the nutritional quality of foods from intensive food production systems has decreased, causing a deficiency of micronutrients in the population [30], so this dimension of food security cannot be accomplished.

Food security also evaluates the performance of food production systems related to optimized cultivation intensity. Nevertheless, the increase in harmful environmental damage has changed how food security measures this indicator. In this sense, the food security framework has added two more dimensions: Agency and Sustainability [26]. The agency promotes compliance with different policies related to food security, especially establishing political frameworks and institutions to defend the

rights of the most vulnerable groups. Sustainability is the dimension that aims to develop adequate management of food systems to contribute to the long-term and present-time regeneration of natural, social, and economic systems so that food demands can be ensured for current and future generations [31].

On the other hand, sustainability has become part of the Sustainable Development Goals (SDGs). In 2021, it was a central objective of the United Nations Summit, where Food Systems issues were discussed. At this meeting, it was emphasized that healthier, more sustainable, and equitable food production systems are required worldwide. For this reason, the search for improvements or development of food production systems has become a priority.

One of the systems proposed in the last years is intercropping; it is a traditional farming system [32] and is considered a diversified and sustainable agricultural technique with optimized cropping intensity.

Many studies show that intercropping can offer different ecosystem services [33] because inputs and natural resources are better used to supply nutrients, which protects plants against pathogens, pests, and weeds. They can also improve soil fertility, conserve biodiversity and natural habitats, and obtain higher yields and more balanced products per unit area from crop diversification [19, 34]. Moreover, it has yet to be discovered that plants included in an intercropping system could increase or decrease the chemical composition of some bioactive compounds and nutrients. The health benefit is related to the possible nutraceutical effect that plant-based foods could obtain during their development in the crop [22, 35, 36]. This can provide the consumer with a greater quantity and quality of nutrients, thus helping to prevent or improve their health status [37], which could benefit the population, especially for communities where food security and health status are compromised.

Therefore, implementing sustainable agroecological systems like intercropping systems could offer a positive environmental impact and produce healthy food, which matches food security policies and SDG.

2.1. Food quality and human nutrition related to food production systems

One of humanity's challenges is developing food production systems that comply with food security.

Health status is closely related to diet and, therefore, to people's nutrition. Nowadays, a correct state of nutrition is affected by different factors, such as the change in people's lifestyles in other regions of the world, which will depend on their technological and economic development [11]. This is why, especially in developing countries, there are different problems related to malnutrition status [38, 39]. These problems are related to the tendency to consume high quantities of fats, sugars, and processed foods with a high caloric density and low in dietary fiber and water since they tend to be foods that are economically accessible to the population. Otherwise, consuming fruits, vegetables, and complex carbohydrates from essential food production in these developing countries is decreasing alarmingly [40, 41]. This food transition also entails an epidemiological transition; the increase in different diseases related to these habits are cardiovascular diseases, various types of cancer, hypertension, type 2 diabetes, polycystic ovary syndrome (PCOS), stroke, and many others associated with overweight and obesity [42, 43, 44, 45]. In general, the population has been told that sufficient and varied consumption of unprocessed foods and lifestyle changes can support the prevention of these diseases. This makes subsistence agriculture for small farmers in developing countries since food and nutritional security depend on it. Still, more than the food produced to feed more people was needed. Intensive monoculture systems were implemented with this objective globally; nonetheless, currently, there is not only a concern about the quantity of food that is produced but also about the nutritional quality of that food [30]. The indiscriminate use of these systems has caused the contents in the edible parts of food crops to have a significant deficit of micronutrients, which means that correct nutrition of the population cannot be guaranteed through the consumption of unprocessed foods or the prevention of chronic degenerative diseases; moreover, this problem could cause what is known as hidden hunger [30]. This is defined as a dietary deficit in the intake of vitamins and minerals; therefore, it is inadequate for optimal human health. In recent years, there have been concerning trends of rising diseases or illnesses in lower-income countries. World Health Organization (WHO) estimates that in 2023 [46], more than a quarter of the global population will be affected by one or more micronutrient deficiencies. The most common deficiencies

of micronutrients registered are vitamin A, iron (Fe), zinc (Zn), and iodine (I) [47]. Micronutrient deficiencies could be a risk factor for many diseases; they can reduce resistance to infections, which can cause severe illnesses, including anemia, mental retardation, blindness, and spinal and brain birth defects [48].

On the other hand, another critical aspect of food security is guaranteeing the safety of the ingested products and the entire process of obtaining that food. Moreover, the first studies about the interaction between agrochemicals and human health are beginning to emerge in different countries. This is related to the intensive application of pesticides [49]. Previously, the damage that exposure to these chemicals could cause to human health was unknown; however, new scientific evidence alerts the population about the indiscriminate use of these substances. The symptomatology of acute poisoning due to excessive use of phytosanitary products such as fungicides and bactericides, herbicides, and insecticides, among others, could be well known; however, the subclinical consequences related to prolonged exposure to these agrochemicals are still little studied. Few studies relate these chemicals to cognitive impairment, reproductive disorders, cancer, diabetes, neurobehavioral and neurodevelopmental disorders, congenital malformations, and cardiovascular, respiratory, and neurodegenerative diseases, such as Parkinson's and Alzheimer's [50, 51, 52]. In addition, there is insufficient control in regulating the use of agrochemicals in some countries, which implies a greater risk for the population [49].

These health problems could be solved by restoring the diversity of agricultural ecosystems, managing crops effectively, and limiting the detrimental environmental effects. Thus, if sustainable production systems are correctly implemented, good nutritional quality will be obtained from the products.

3. Modifying the nutritional profile in intercropping systems

Backyard production is plants managed in traditional land use systems in areas close to homes in developing countries [53]. Implementing these spaces promotes the cultivation of multiple species to ensure basic needs [54], providing most of the daily nutrients to families. It is a critical practice in situations of food scarcity [55, 56]. Plant seeds and edible parts of the plant are considered nutrient-rich food sources of great importance for human nutrition. They contain ample amounts of numerous essential nutrients: lipids, peptides/proteins, amino acids, starch, dietary fiber, vitamins, and minerals [57]. Likewise, some bioactive compounds are derived from the plant's seeds, fruits, roots, and leaves; they are phytochemicals like phenolic compounds (tocopherols, flavonoids, and phenolic acids), nitrogen compounds (alkaloids, chlorophyll derivatives, amino acids, and amines), carotenoids, or ascorbic acid, quinones, terpenoids and saponins [58, 59].

In recent years, consumer demands have changed to sustainable food production, similar to agricultural techniques in family gardens [60]. Interest in food quality, functional foods, eating seasonally, locally, and organic has been growing [12, 61, 62]. This is why the search for crops with highly nutritional species has been a challenge worldwide [63]. The "sustainable diet" is a term that was established after sustainable food production; this concept includes all dimensions of people's health and well-being because it has a low environmental impact and is accessible, affordable, safe, and equitable, which it also complies with the dimensions of food security [13]. Moreover, this sustainable diet conserves traditional regional cuisine as a part of the intangible heritage of societies and communities, and it is a fundamental point of regional and local economies [64].

Mixed cropping, as part of sustainable agriculture, can support low-income households to afford a more diverse diet, taking advantage of daily intake of essential foods. Combinations of cereals, legumes/seeds, and oilseeds in intercropped systems can provide a large part of the caloric intake of these families [14]; therefore, these systems have a vital role in alleviating hunger, primarily if these systems are implemented with the potential to influence in the amounts of nutrients and bioactive phytonutrients [63]. Nevertheless, just a few studies have been taking place intending to implement intercropping systems to improve the nutritional quality of the species in the crops.

Within the studies that reviewed the nutritional quality and quantity of bioactive compounds and macronutrients that can be modified using intercropped systems, different countries have implemented these systems according to their dietary needs and species of interest. It is interesting to analyze the methodology carried out within these studies and the modified nutrient type. It is known that food quality depends on genetic factors, environmental conditions, growing location,

and agronomic practices. Tables 1, 2, and 3 combine the most relevant characteristics of various investigations where an intercropped system was implemented to modify the nutritional profile of one or more species involved to benefit human nutrition.

In this context, there are studies where importance was given to the modification of bioactive compounds, others to the change in the quantities of other nutrients, and others to search both profiles.

3.1. Intercropping systems with cereals and legumes

In general, the intercropping of cereals and legumes is a global practice. It has been widely used to increase crop yield due to the nitrogen (N) biological fixation. Still, in recent years, various investigations have discovered that this method could cause crude protein to arise in one or both species. This improvement is related to N and phosphorus (P) transfer from the legume to cereal during their co-growing period in these intercropping systems [65, 66, 67, 68].

Table 1. Research where an intercropping system was implemented to modify both bioactive compounds and macronutrients content of one or more of the species involved for the benefit of human nutrition.

Species involved	Methodology	Bioactive compounds	Macronutrients	Country or climatic zone	Author/ year
Maize and peanut	Six treatments with 2 intercropping systems maize-pea and maize -soybean with and without application of fertilizer and their respective monocultures and each treatment was replicated three times. Plot area: 33 m ² (6 m × 5.5 m) and the field experiment had a total of 18 plots.	Maize intercropping (peanut and soybean) increased lysine content of maize grains when no fertilizer was applied. When fertilizer was applied in both intercropping systems the content of lysine increased.	Maize intercropping (peanut and soybean) significantly increased protein and oil content of maize grains when no fertilizer was applied. When fertilizer was applied in both intercropping systems the content of starch increased.	China	[69]
Maize and soybean					
Barley and alfalfa	An intercropping pot experiment with AMF and PGPR. Three inoculation treatments (for both mono-cropped and intercropped plants) and the control were used:	Intercropping and co-inoculation of AMF+PGRPR increased total phenolic 132%, and flavonoid 343% content of barley grains.	Intercropping and co-inoculation of AMF+PGRPR increased protein in 99%.	Marrakesh, Morocco	[83]

(1) AMF-inoculated plants; (2) PGPR-inoculated plants; (3) AMF+PGPR co-inoculated plants

A study carried out with a maize-peanut intercrop and another maize-soybean combination compared to a maize monoculture, with or without fertilizer application, sought to determine the quality of the maize grain in terms of its starch, protein, oil, and lysine content. The economic performance, the abundance of microorganisms, and the activity of various enzymes were also reviewed. The results showed different amounts of nutrients (maize grains' protein, oil, and lysine content) depending on whether and type of fertilizer was used (Table1), in general intercropped show an increment of some nutrients. Finally, nitrogen fertilizer did not substantially affect the intercropping outcome of maize grains' starch, protein, and lysine content [69].

Table 2. Research where an intercropping system was implemented to modify the macronutrient content of one or more of the species involved for the benefit of human nutrition.

Species involved	Methodology	Macronutriments	Country or climatic zone	Author/Year
Wheat and faba bean	Intercropped wheat and faba bean with (N) fertilization: N0, no N fertilizer applied to both wheat and faba Bean. N1, 90 and 45 kg N ha ⁻¹ applied to wheat and faba bean. N2, 180 and 90 kg N ha ⁻¹ applied to wheat and faba bean. N3, 270 and 135 kg N ha ⁻¹ applied to wheat and faba bean. Group control: Wheat and faba bean monoculture	Wheat grain protein content increased by 9% with N3 level, NEAAs content was 31% higher under the N1 level and, grain EAAs was increased by 39% at the N1 level relative to monoculture wheat.	China	[68]
Spring wheat and different legumes	Two basic systems were compared mixture and row-by-row cropping in 3 different locations.	The row-by-row cropping system resulted the higher crude protein content (14.02%) than the mixture (13.79%). Zvhad (Zv) had the	Czech Republic; Prague (PR), Uhříněves (UH) and Zvíkov (Zv).	[70]

		highest crude protein content (15.14%).		
Wheat and clover	2 types of trials: The "Broadcast" with three treatments: unfertilized system, where wheat was sown in paired rows (330 seeds m ⁻² , 21%) and clover was broadcast sown (1250 seeds m ⁻² , 79%) (Pcwbc); unfertilized wheat as a sole crop, sown in paired rows (330 seeds m ⁻²) (Ctrlpr); wheat as a sole crop, sown in single rows (440 seeds m ⁻²), and fertilized with organic poultry manure (Ctrl). The "Row" trial with three treatments: unfertilized system, where both wheat (330 seeds m ⁻² , 21%) and clover (1250 seeds m ⁻² , 79%) were sown in paired rows (Pcw); the Ctrlpr (330 seeds m ⁻²) and Ctrl (440 seeds m ⁻²) treatments, as in the "Broadcast" trial	Wheat grain protein content was 16% and 24% higher in Pcw and Pcwbc, respectively, than in Ctrlpr, and 15% and 28% compared to Ctrl.	Surrounding of Pisa (sites: Valtriano and Santa Luce	[81]

A two-year experiment in China (Table 2) reveals that grain protein contents could improve in wheat and faba bean intercropping. In this case, not just the percentage of grain protein contents were enhanced; moreover, the quantities of non-essential and essential amino acids were improved under different nitrogen input conditions [68]; another study that took place in 3 other location in the Czech Republic (Prague, Uhřetěves and Zvíkov), also investigate the grain protein content in wheat intercropped with Egyptian clover, crimson clover, red clover, white clover, common pea, dun pea, common vetch, bird's-foot-trefoil, common kidney vetch, and fenugreek with two different intercropping crops (mixture and row-by-row cropping) [70] (Table 2). The increase of spring wheat crude protein content cropped with legumes was higher by 12%.

Another intercropping system that involves cereal and legumes is Milpa, which is a polyculture, where mainly maize (*Zea mays*), beans (*Phaseolus spp.*), and pumpkin (*Cucurbita spp.*) grown together in different topological arrangements and different associated species, depending on the region where is implemented. This intercropped system has been analyzed for various ecological and yield proposes [39, 71]. However, in recent years, it has been highlighted that this food production system has a critical role as a source of food and nutritional security because it provides both macro-nutrients (fat, protein, starch) and micro-nutrients (vitamins and minerals) [72]. Moreover, many milpas

studies examine food yields from a different perspective; for example, a survey carried out in North America with the Iroquois group defined the quantities of energy (12.25 x 106 kcal/ha) and protein (349 kg/ha) produced per unit land area, comparing them with crop monocultures or mixtures of monocultures planted to the same area [73]. Furthermore, other studies show that milpa systems produced significantly more essential nutrients beyond yield and calories. Similar results were found in a Mayan milpa system, and this research measured the agricultural products and nutritional content of all harvested from a traditional Lacandon milpa. They found out that for an average family size of 5 individuals, this intercropping can meet most United States Food and Drug Administration (FDA) daily value nutritional requirements per capita of calories, fat, carbohydrates, fiber, protein, vitamins A and C, calcium, iron, zinc, and niacin [72]. Likewise, the Western Highlands of Guatemala is one of the world's poorest regions, and food insecurity and malnutrition affect more than half of its inhabitants [74]. A study in this area took place to calculate the potential number of people fed (PNPF) considering the essential components of human nutrition, the nutrient concentrations in the common edible parts of the raw crops, and the amounts of each crop produced.

Moreover, the maize-bean-faba, maize-potatoes, and maize-bean-potatoes associations had the highest PNAs, (Potential Nutrient Adequacy), contributing the most carbohydrates, proteins, zinc, iron, calcium, potassium, folate, thiamin, riboflavin, vitamin B6, niacin and vitamin C [75]. Some review and research articles on bioactive compounds involved in milpa systems have recently been published because of the interest in beneficial substances beyond human nutrition. In these studies, they analyzed the bioactive and chemical composition [39, 76, 77,] of the species involved and others studied the nutritional and health benefits of milpa system seeds assessed by recent preclinical and clinical trials [78].

Table 3. Research where an intercropping system was implemented to modify bioactive compounds content of one or more of the species involved for the benefit of human nutrition.

Species involved	Methodology	Bioactive compounds	Country or climatic zone	Author/year
Milpa (colored corn, climbing bean, and squash, tobacco) with potato, 3 classes of peppers, namely poblano, jalapeño, bell pepper, beetroot, carrot and kale.	All vegetables were first grown in greenhouse, except potato tubers were directly planted in the garden plots. 45-day-old seedlings were transplanted at Probstfield Organic Community Garden. No chemical fertilizers were used for this study.	Kale had the highest total soluble phenolic (TSP) content with 1.02 mg/g FW. He also had the most elevated phenolic acids, detecting dihydroxybenzoic acid, ferulic acid, and cinnamic acid. Among the three classes of peppers, jalapeno (gallic acid and p-coumaric acid) and poblano (benzoic acid, dihydroxybenzoic acid, and catechin) they had higher concentrations of phenolic acids.	Northern plains USA	[80]
Fenugreek Seeds with Buckwheat	Two year experiment with Four treatments:	Results in intercropping fenugreek seeds:	Iran	[82]

	<p>Sole fenugreek (control) with 3 intercropping ratios with buckwheat; F:B = 2:1, 1:1, and 1:2 each with three types of fertilizer (chemical fertilizer, integrated fertilizer, and broiler litter. They investigate the trigonelline content, antioxidant activity measured with DPPH and FRAP, total phenolic and flavonoid content, and specific flavonoid contents of fenugreek seeds</p>	<p>-Antioxidant activity: Higher DPPH levels, on average, by 12.3% (2014) and 12.5% (2015) compared to Sole F, so the antioxidant activity increased. The highest antioxidant activity was measured in the F:B = 2:1 plots with 4.25 (2014) and 4.90 (2015) mg TE/g DW.</p> <p>-Total phenolic content: Average 8.00% (2014) and 3.33% (2015) higher compared to the Sole F.</p> <p>Total flavonoid contents: On average, 32.4% (2014) and 23.8% (2015) higher than in seeds harvested from Sole F.</p> <p>-Flavonoids compound content</p> <p>Vitexin content was higher on average 40.2% (2014) and 17.5% (2015) than for seeds from Sole F.</p> <p>Isovitexin content was on average, 14.9% (2014) and 9.88% (2015) higher than in Sole F.</p> <p>Orientin content was higher on average, 23.1% (2014) and 15.5% (2015) compared to Sole F.</p>		
<p>Tomato and basil, cabbage plants</p>	<p>Two systems compared with commercial control (cv. Rio Grande):</p>	<p>The LI system showed a higher content of polyphenols (+37.9%) and anthocyanins</p>	<p>Italy</p>	<p>[36]</p>

	LI; system involved the application of cow manure and manual weed control. LIMI; the same system was integrated (LI) with mulching and intercropping (basil and cabbage plants). Both systems integrate line 392, harboring the hp-2 gene that increases the pigments of plant and fruit; the line 446 with the <i>atv</i> and <i>Aft</i> genes which influence the content of polyphenols.	(+116.7%) in the peel and a higher content of vitamin C (+44.0%) and polyphenols (+11.1) in the pulp		
Salicornia europaea and tomato	The experimental design forecasted three different kinds of plots, namely Salicornia in monoculture (S) (double rows of twenty-five plants each), Salicornia consociated with tomato plants (S-T) (two rows of thirteen tomato plants each, with twenty-five Salicornia plants planted at each side of the two tomato rows, and tomato in monoculture.	The cultivation method (intercropping-monoculture) had no effect on the concentration of fatty acids, chlorophylls, carotenoids, glycine betaine, total phenols, tannis, except for flavonoids that did decrease its concentration (-26%) in intercropped.	Italy	[23]

All these investigations are related to the nutrients that are available in this system since more species are involved; however, the interest in studying the possible changes in the production of bioactive compounds like alkaloids, terpenoids, phenolic compounds, and steroids, and other nutrients through interactions between the species in the milpa system has increased. This interest is related to bioactive compounds and bio-functional properties like anti-inflammatory, antiproliferative, antimicrobial, antibacterial, antifungal, and anticancer used for therapeutic applications in human health [79], also since it is the most popular polyculture system in Mesoamerican countries. In 2017, a milpa procedure of colored corn, climbing bean, squash, and tobacco with potato, three classes of peppers, namely poblano, jalapeño, bell pepper, beetroot, carrot, and kale (Table 3), was carried out to recover American Indians group health, due to growing

prevalence of non-communicable chronic diseases (NCDs) in this community, such as type 2 diabetes (T2D), by integrating bioactive-enriched vegetables. Since the purpose was to seek a positive impact on the health of this community, tests were carried out to review the Anti-hyperglycemic and Anti-hypertensive properties of the vegetables used. In all cases, kale has the highest α -amylase and ACE inhibitory activity, related to the quantity and quality of phenolic acids and total antioxidant activity (ABTS and DPPH) [80]. It is essential to point out that this is the only study that evaluates the effect of the bioactive compounds in its intercropping system.

3.2. *Intercropping cereals with herbaceous plants*

A cereal intercropped study with wheat and clover (Table 2) obtained higher amounts of grain protein, and the experiment involved using fertilizers and unfertilized systems. A higher grain protein was obtained with an unfertilized system where wheat was sown in paired rows, and clover broadcast sown [81]. Another experiment studied the effect of an intercropping system with fenugreek and buckwheat on the trigonelline content, antioxidant activity measured with DPPH (2,2-Diphenyl-1-Picrylhydrazyl) and FRAP (Fe⁺⁺⁺-Reduction, Ferric reducing antioxidant power), total phenolic content, total flavonoids content, and specific flavonoid contents of fenugreek seeds (Table 3). One of the intercropped treatments enhanced the antioxidant activity and the content of bioactive compounds, and in general, fenugreek seeds that were intercropped with buckwheat (organic fertilizer) enhanced the seed content of antioxidants and flavonoids. The authors explained that the increase in antioxidant activity could be caused by the overall promotion of organic manure in supplying macro- and micro-nutrients responsible for antioxidant activity [82].

In other research, barley and alfalfa intercropping was combined with beneficial microorganisms, arbuscular mycorrhizal fungi (AMF), and plant growth-promoting rhizobacteria (PGPR) (Table 1) both to improve crop yield and soil health and to increase some nutrients. In this context, an experiment was carried out where inoculation with arbuscular mycorrhizal fungi (AMF) and plant growth-promoting rhizobacteria (PGPR) was carried out in barley and alfalfa plants. Favorable barley yield results were obtained, and the soil's nitrogen and phosphorus contents improved. Moreover, there was also an increase in the protein, total phenolic, and flavonoid content of the barley grains [83].

3.3. *Intercropping without legumes and cereals*

There are other intercrops where neither legumes nor cereals have been used, and it has been possible to change the amount of bioactive compounds. It is worth mentioning that not all studies obtained favorable results to produce bioactive compounds. However, it is important to review the reasons. In a tomato and basil cabbage plants intercrop study, yield and bioactive compounds were analyzed in the pulp and peel of the tomato fruits. Intercropping did not produce good results to produce bioactive compounds (Table 3). Only the non-intercropped system had an increase in bioactive compounds. The authors related these results to the biotic and abiotic stress between the species [36].

Another tomato intercropping system combined with *Salicornia europaea* (Table 3) evaluates the nutritional profile and the content of some health-promoting compounds of the edible portion of *Salicornia europaea*. Additionally, the antioxidant, antibacterial, and anti-inflammatory properties of *S. europaea* were studied to characterize its bioactivity. The cultivation method did not affect nutrients and bioactive compounds, except for flavonoids, where the intercropping system's content decreased. Nonetheless, the potential protective effect of *S. europaea* methanol extract against TNF and the bioactive components like cyanine, isoflavones, flavanones, etc. These findings proved antioxidant and anti-inflammatory activity and neuroprotective properties can be developed in this intercropping system [23].

4. Another Approach for improving nutritional profile in intercropping systems

Sustainable agriculture can encompass various agricultural techniques, significantly affecting food production. This is a latent concern since these systems must satisfy human needs while respecting natural resources [84].

In the arduous task of finding the ideal conditions for multiple cropping systems, several studies have been conducted, and some researchers have already collected valuable information. A review

in 2015 gathered several studies about the biotic interactions that could be met in different polyculture systems to provide more ecosystem services. It also offers information on how to implement polyculture step by step based on another research [17]. These guidelines for designing multiple cropping systems combine ecological, agricultural, and genetic concepts and approaches. A similar review in 2021 emphasizes the features that must be reviewed to implement intercropping strategies to enhance food and environmental security. This study also highlights the importance of different factors, such as the choice of crops and cultivars, sown proportions, and agronomic management, including water and nutrients [14]. Neither review shows an approach to change nor ameliorate the nutritional profile of the crops for human benefit. However, both studies conclude one latent problem where part of the research can be focused on improving the nutritional profile of the edible parts in this type of system; they talked about the availability of trait values of cultivars and specific eco-physiological models for an adequate construction of an ideotype.

Moreover, adequate construction of the ideotype is necessary for the competitive capacity of the crops to affect both the yield and the success of intercropping systems [17, 14]. In this sense, research related to the immune system in plants is crucial. Integrating the metabolic pathways associated with producing secondary metabolites and the type of stress that activates them is vital. Both the adaptive (eustress) and non-adaptive (distress) response to stress can significantly influence the effective channeling of plant energy into biomass production or the bioactive profile [85, 86].

5. Materials and Methods

The articles in this review were found thanks to keywords like food security, intercropping, bioactive compounds, grain quality, nutrient profile, sustainable agriculture, human health, eco-physiology, and phytochemical properties. Ninety-two research and review articles were consulted for this document in different sources (MDPI, Taylor and Francis, Research Gate, Springer, Google Academic, Cross reference, Science Direct).

More specifically, nine articles were classified on different tables. These tables included investigations of intercropped systems that aimed to improve the nutritional profile of one or more species involved in human nutrition. According to the methodology implemented, were classified according to the types of nutrients that were sought to be improved, so Table 1 is intended for research in which there was an improvement in the quantities and quality of both bioactive compounds and macronutrients; Table 2 for macronutrients and table 3 for bioactive compounds.

The studies that did not meet these conditions were not considered for developing this portion of the document. However, some are mentioned in other sections since they contain critical points for the adequate development of intercropped systems that seek to improve food security.

6. Conclusions and future perspectives

To the best of our knowledge, this is the first study that brings together the research carried out to date on intercropped systems that had the purpose of modifying nutrients and bioactive compounds profile of the species involved for human health. Some of these investigations obtained favorable results in modifying the amounts of either bioactive compounds, some macronutrients, or even both. On the other hand, in further studies, the different treatments implemented in intercropping did not affect these indicators.

Even though one of the main objectives of the SDG is to improve the quality of food for the benefit of human consumption through agroecological systems, several discrepancies still need to be found. In general, the research related to nutritional profiles in intercropped systems for human health needs to be more scattered. Nevertheless, we still need to consider the possibility that there are more studies related to this topic in other sources. Although we find articles in which the type of species is repeated, there is no clear explanation why such an association was implemented, neither the physiology nor allelopathic interaction. More studies related to this topic are necessary to influence the metabolic pathways of interest to produce specific bioactive compounds to be able to test their bioactivity on human health subsequently. About the above, the content of bioactive compounds of several species grown in monoculture is being reviewed more effectively to obtain a nutraceutical benefit in humans [39,78,87], which could be the basis for understanding more metabolic pathways with the different types of stress that activate them and will be helpful to compare and improve the amount of these bioactive compounds or macronutrients in intercropped

systems under other conditions. In these studies, the possible change in some organoleptic characteristics, such as the taste (bitter) of foods in which bioactive compounds have been increased [88], has been mentioned. This characteristic opens a panorama of the different research topics that may arise from implementing polyculture systems.

Likewise, yield and environmental benefits associated with intercropped systems should be addressed, even if the primary goal is to improve human nutrition. Most of the studies reviewed did not leave aside these characteristics since there is enough information to support the benefits that these polycultures bring to the environment and that there is indeed an improvement in yield, even the techniques have been improved by adding different types of fertilizers and microorganisms, thanks to these agroecological technics soil health and nutrient management is more adequate [4, 69, 79]. These same techniques should also be studied more regarding the effect on the phytochemical profile of the plants.

Furthermore, it is important to add that little has been studied about the importance of using regional species in intercropping. Some studies prove its effectiveness in reestablishing biodiversity and natural habitats according to their level of adaptation to the different ecoclimatic conditions of the areas where they are located [89, 90]. There are even some articles where the development of nutraceutical properties was found [80]. These points are of great value to study since the development of a sustainable diet is based on obtaining the most significant possible benefits from different socioeconomic and environmental perspectives without losing the culinary and cultural customs of the region, which is important for food security worldwide [91].

Finally, the answer to whether we have the necessary information to develop intercropping systems to benefit human health must be answered from various perspectives. There are different studies where the bases can be found to be able to implement intercropped systems with this objective. However, it is necessary to analyze all this information with the plant's ecophysiology and immunity (hormetic response) that will interact in polyculture to formulate new theories and thus establish an adequate construction of the ideotype [85, 92]. This would contribute to producing foods with a proper nutritional profile and even to obtain a benefit that goes beyond conventional nutrition to impact food security and the population's health status positively.

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