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RESEARCH

Public perception of folate-biofortified genetically modified lettuce varieties in Brazil

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Abstract Lettuce is one of the most widely consumed vegetables in the world, commonly eaten fresh in salads, sandwiches, wraps, and as a garnish in various dishes. Consequently, it is a very promising vehicle to deliver vitamins, such as folate (vitamin B9), to a specific population using biofortified varieties generated by conventional or molecular breeding. A new genetically modified lettuce was generated with increased folate content. However, some issues related to public perception regarding this technology should still be evaluated. The aim of this study was to analyze whether consumers are willing to accept a folate-biofortified GM lettuce that could become available to the Brazilian market. A questionnaire involving several issues regarding lettuce consumption was answered by 2,391 people from almost all Brazilian states. When informed that the folic acid biofortified lettuce is a transgenic plant, 46.1% of respondents stated that they would eat it and 30.5% stated that it would be a possibility. This study demonstrated that if there is any explanation regarding the advantage in relation to the use of biotechnology, like enrichment with folic acid, the number of people who accept it increases.

Keywords Biotechnology · Folic acid · Healthcare · Public acceptance · Transgenic lettuce

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Introduction

Lettuce (*Lactuca sativa* L.) is one of the most widely consumed vegetables in the world, and its production is a significant component of global agriculture, cultivated in numerous countries across the world. The top lettuce-producing countries include China (14.3 million tons), the United States (3.4 million tons), India (1.1 million tons), Spain (1.1 million tons), and Italy (9.6 million tons) (FAOSTAT 2021). It can be grown in open fields, greenhouses, and hydroponically, using conventional or organic farming systems (Ahmed et al. 2021; Cámara-Martos et al. 2021; Wang et al. 2023). There are several types of lettuce, but the most commonly grown varieties worldwide include iceberg, romaine (cos), butterhead, and loose leaf. The popularity of lettuce is due to its crisp texture, mild flavor, and high-water content, making it a refreshing and healthy addition to meals (Kim et al. 2016; Shi et al. 2022). It is a low-calorie vegetable (5–10 cal per 100 g) that offers a range of essential nutrients, such as carbohydrates, vitamins (A, K and C), minerals

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(iron, potassium and calcium) and antioxidants (flavonoids) (Kim et al. 2016; Medina-Lozano et al. 2021; Shi et al. 2022; Yang et al. 2022). Since lettuce is commonly eaten fresh in salads, sandwiches, wraps, and as a garnish in various dishes, it is a very promising vehicle to deliver vitamins, such as folate (vitamin B9) to a specific population using biofortified varieties generated by conventional or molecular breeding. This is a sustainable and cost-effective method to improve public health, particularly in regions where people rely heavily on a limited number of staple crops. Folate is an essential nutrient that supports various bodily functions, such as cell division and DNA/RNA synthesis, red blood cell formation, synthesis of neurotransmitters like serotonin and dopamine, methylation reactions, repair of damaged DNA and gene regulation (Birla et al. 2022; Nascimento et al. 2022; Nogueira-de-Almeida et al. 2023). Its deficiency is associated with several important diseases, such as anemia (Roche et al. 2021), depression and cognitive decline (Jin et al. 2022a, b), risk of stroke (Zhang et al. 2022), erectile dysfunction; Feng et al. 2023) and prostate cancer (Bailey et al. 2015). Folate is also crucial for preventing neural tube defects in the developing fetus, which affect around 1 in every 1,000 pregnancies worldwide (Mitchell 2005; Tsiklauri et al. 2019; Li et al. 2020).

In this context, we increased folate content in lettuce by expressing *Arabidopsis thaliana* genes coding for enzymes of the folate biosynthesis pathway (Nunes et al. 2009). However, although 2.7 billion cumulative hectares have been cultivated worldwide with genetically modified (GM) crops (transgenic) since 1996 (ISAAA 2019), there are some issues related to public perception that should still be evaluated. Perception varies widely around the world and is influenced by cultural, social, economic, and political factors. It was observed that the acceptance of GM crops is dependent on the level of education and knowledge of the people on the subject. More than two hundred university students in India responded to a survey to investigate their knowledge and attitudes about GM foods. Most of the participants agreed to have read about GM foods and defined it correctly. It was observed that attitudes in favor of GMO were related to higher knowledge scores (Rathod and Hedaoo 2022). Furthermore, when people are informed about the benefits of growing and consuming GM foods, they tend to be more positive. When Swedish consumers were questioned about various GM foods technologies, most of them had a negative attitude towards it. However, information on potential benefits, such as less agricultural impact on the environment, better taste or lower price was enough to persuade them to purchase GM foods (Magnusson and Hursti, 2002). In a public perception involving Chinese consumers, it was observed that perceived benefit is a major factor shaping GM product-specific acceptance, and perceived risk is not as influential as previous studies have suggested (Jin et al 2022a, b).

While biofortification holds great promise, there are challenges to its widespread adoption, including the need for public awareness and acceptance and adoption by farmers. The aim of this research is to analyze whether consumers are willing to accept a folate-biofortified GM lettuce that could become available to the Brazilian market. This type of research is important because consumers are extremely important economic agents in the command hierarchy of technological innovation in food production chains. Any type of agronomic research aimed at technological innovation should carry out research of this type in the "real world", which is complex and full of cultural, economic, marketing, social and political variables.

Materials and methods

Data collection.

The data were collected using the online survey (Google forms platform) in Brazil. The form remained open for response for 17 days in 2023. The respondents gave consent and were recruited by an online panel provider. They were informed that no data could be linked to individual participants and would be anonymously analyzed. In order to follow the Brazilian and international ethical codes, only respondents aged 16 years old or over were taken into consideration. The questionnaire took approximately 4 min to be completed. Pilot testing was previously carried out to verify the time to answer the questions and data collection method.

The sociodemographic characteristics surveyed include: state of residence, age and education level. We chose not to ask about the family's monthly income because we assumed it would be an inhibiting question. Thus, the main social variable consisted

of the educational level. On the other hand, there is no unanimity regarding the delimitations of social classes in Brazil. Therefore, the only solution we found was to ask about the educational level. The questionnaire consists of 12 multiple-choice or yes/no/maybe questions (Table 1), originally written in Portuguese. It is important to highlight that the research was carried out using "snowball" sampling. “Snowball” sampling consists of identifying some key informants who are willing to collaborate by answering the questionnaire. At the end of the answers, each participant indicates new informants, until a saturation point is reached, with no more new people willing to respond (Parker et al. 2019).

Table 1 Questionnaire content (English and Portuguese versions)

Questions / answers	Questões / respostas
Which state in Brazil do you live in? List of the 27 Brazilian states	Você mora em qual estado do Brasil? Lista com os 27 Estados do Brasil
How old are you? Free response	Qual é a sua idade? Resposta livre
What is your educational level? Incomplete elementary education Complete elementary education Incomplete high school Complete high school Incomplete college / university Complete college / university Master’s degree Doctoral degree	Qual é o seu nível de escolaridade? Ensino Fundamental Incompleto Ensino Fundamental Completo Ensino Médio Incompleto Ensino Médio Completo Superior Incompleto Superior Completo Mestrado Doutorado
What is most important when you buy lettuce? Being organic Being sanitized and packaged Looking good Lower price	O que é mais importante quando você compra alface? Ser orgânica Estar higienizada e embalada Ter boa aparência Preço mais baixo
Do you think the price paid for a head of lettuce is… Cheap Expensive	Você acha que o preço pago por um pé de alface é: Barato Caro
How many times per week do you eat lettuce? every day once or twice more than three times never	Quantas vezes você consome alface por semana? todos os dias uma ou duas vezes mais de três vezes nunca
What type of lettuce do you prefer? loose leaf butterhead iceberg purple i don’t consume	Qual é o tipo de alface que você prefere? crespa lisa americana roxa não consumo
Do you know the vitamin folic acid? Yes / No	Você conhece a vitamina ácido fólico? Sim / Não
Do you know the importance of the vitamin folic acid for health? Yes / No	Você sabe a importância da vitamina ácido fólico para a saúde? Sim / Não
Would you buy lettuce with a higher amount of folic acid? Yes / No / Maybe	Você compraria alface com maior quantidade de ácido fólico? Sim / Não / Talvez
Knowing that folic acid is good for your health, would you choose lettuce with more of this vitamin? Yes / No / Maybe	Sabendo que o ácido fólico é bom para a saúde, você escolheria uma alface com mais dessa vitamina? Sim / Não / Talvez
Would you eat transgenic lettuce with more folic acid? Yes / No / Maybe	Você comeria alface transgênica com mais ácido fólico? Sim / Não / Talvez

Statistical analysis

The statistical analyses were carried out using Prism 6 for Windows software. Correlation analyses [age versus product conditions (i.e. being organic, being sanitized and packaged, looking good, having a lower price) and choosing organic versus accepting or refusing consumption of the transgenic lettuce] were calculated using Pearson's correlation coefficient at 95% confidence interval.

Results

The questionnaire was answered by 2,391 people from all Brazilian states, except Amapá, over a period of 17 days. Most of the respondents live in the Midwest region (38.1%), followed by the Southeast (33.7%), Northeast (18.9%) South (6.7%), and North (2.7%) regions (Fig. 1). Persons from 16 to 95 years old responded to the questionnaire, with concentration in the group of 56 to 60-year-olds (12.3%), followed by 51–55 (12%), 46–50 (9.7%), 36–40 (9.5%) and 41–45 (8.9%) (Fig. 2). A total of 266 people did not declare their age. The majority of the surveyed participants presented a higher education level, with 43.5% having completed college / university courses, 17.2% holding a doctoral degree, 14.5% a master's degree and 11% still attending college / university courses (Fig. 2). It is important to highlight that this means that the majority have a very high level of education, which corresponds, in Brazil, to the upper-middle class. Most of the respondents prefer to consume lettuce once or twice a week (39.9%) or more than three times a week (35.4%), while 22% consume it every day. Just 3.9% never consume it (Fig. 3A). In addition, most respondents prefer iceberg varieties (47.7%) followed by loose leaf (28.4%), butterhead (19.6%) and purple (3.7%) (Fig. 3B). Respondents mentioned that a good appearance (56.6%, looking good) is the most important factor, followed by being well sanitized and packaged (21.8%). Organic lettuce was also a relevant factor (19.9%) (Fig. 3C). Surprisingly, the price relevance was only mentioned by 1.6%. In fact, when specifically questioned if the price paid for a head of lettuce is cheap or expensive, 67.2% responded that they consider it cheap, while 32.8% believe it is expensive (Fig. 3D). We found

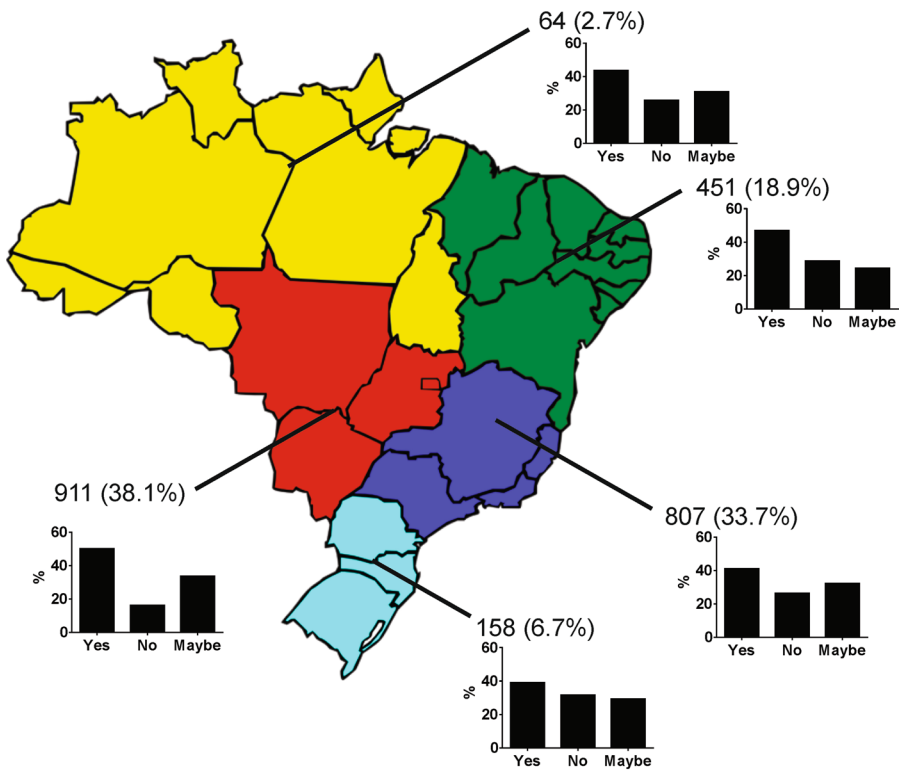

Fig. 1 Number (and percentage) of respondents in the North (yellow), Midwest (red), Northeast (green), Southeast (dark blue) and South (blue) Brazilian political regions. Graphs show the percentage of respondents in each region that answered "Yes", "No" or "Maybe" when questioned if they were willing to consume a transgenic variety of folic acid-biofortified lettuce. North, Midwest, Northeast, Southeast and South regions compose 8.4%, 7.4%, 27.8%, 42.1%, and 14.3% of the Brazilian population, respectively

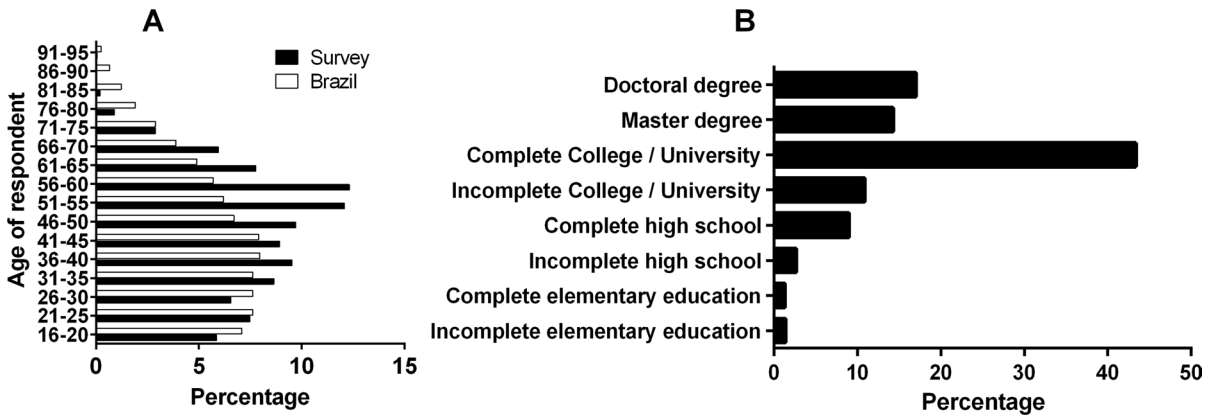

Fig. 2 Histograms showing the age distribution **A** and educational levels of participants **B**. Brazilian data was retrieved from https://censo2022.ibge.gov.br

no statistically significant correlation between age and product conditions (being organic, being sanitized and packaged, looking good or having a lower price) (Pearson´s correlation, $\alpha = 0.05$). The majority of the surveyed respondents know folic acid (73.6%) and responded that they are aware of its importance for health (62.8%) (Fig. 3E-F). When it was informed that folic acid-biofortified lettuce is a transgenic plant, the number of respondents who stated that they would eat it was 46.1%, with a group saying that maybe they would eat it (30.5%) and 23.4% stating that they would not consume it (Fig. 3G). Furthermore, 49.8% would prefer a lettuce variety biofortified with folic acid, and 44.5% responded that maybe they would buy it. Just 5.7% stated that they would not buy it (Fig. 4A). Of those 49.8% that answered "Yes" when questioned if they would choose the biofortified lettuce, 45.6% would still prefer to eat it (and 31.9% said maybe; 22.5% said No), if they knew it is a transgenic plant. On the other hand, from those 44.5% that answered "Maybe" to that question, 44.3% would accept it (Yes), when informed that it is transgenic (Fig. 4A). Surprisingly, of those 5.7% that answered that they would not buy the biofortified-lettuce, 59.7% of them said they would accept it if transgenic (Fig. 4A).

When informed that folic acid is good for health, the number of consumers that would choose lettuce varieties enriched with this vitamin rose to 74.5%, while 21.3% stated that perhaps they would buy it and just 4.2% said that they would not buy it (Fig. 4B). Of those 74.5% that answered "Yes" when questioned if they would choose the biofortified lettuce, knowing that folic acid is good for health, 46.4% would still prefer to eat it (and 32.1% maybe), if they know it is a transgenic plant. On the other hand, from those 21.3% that answered "Maybe" to that question, 40.7% would accept it, when they are informed that the biofortified varieties are transgenic. Surprisingly, among those 4.2% that answered that they would not choose the biofortified-lettuce, 60.4% would accept it, when informed that it is transgenic (Fig. 4B).

In general, people are willing to consume genetically modified biofortified lettuce in all Brazilian regions (Fig. 1). We found no statistically significant correlation between choosing organic and accepting or refusing consumption of the transgenic lettuce plants (Pearson´s correlation, $\alpha = 0.05$). The proportion of supporters was higher in the Midwest region (47.2%), followed by the Northeast (41.8%) and North (38%) regions. In addition, the number of respondents answering "maybe" was also relevant in all regions (Fig. 1), but was higher in the Midwest region (33%), followed by Southeast (31.4%) and South (28.8%) regions.

Discussion

There are many players involved in the use of modern biotechnology (Aliev & Kurbanova 2022; Munaweera et al. 2022). There are supporters, skeptics and opposition groups. Among the supporters, there are the scientists and experts in the field of biotechnology

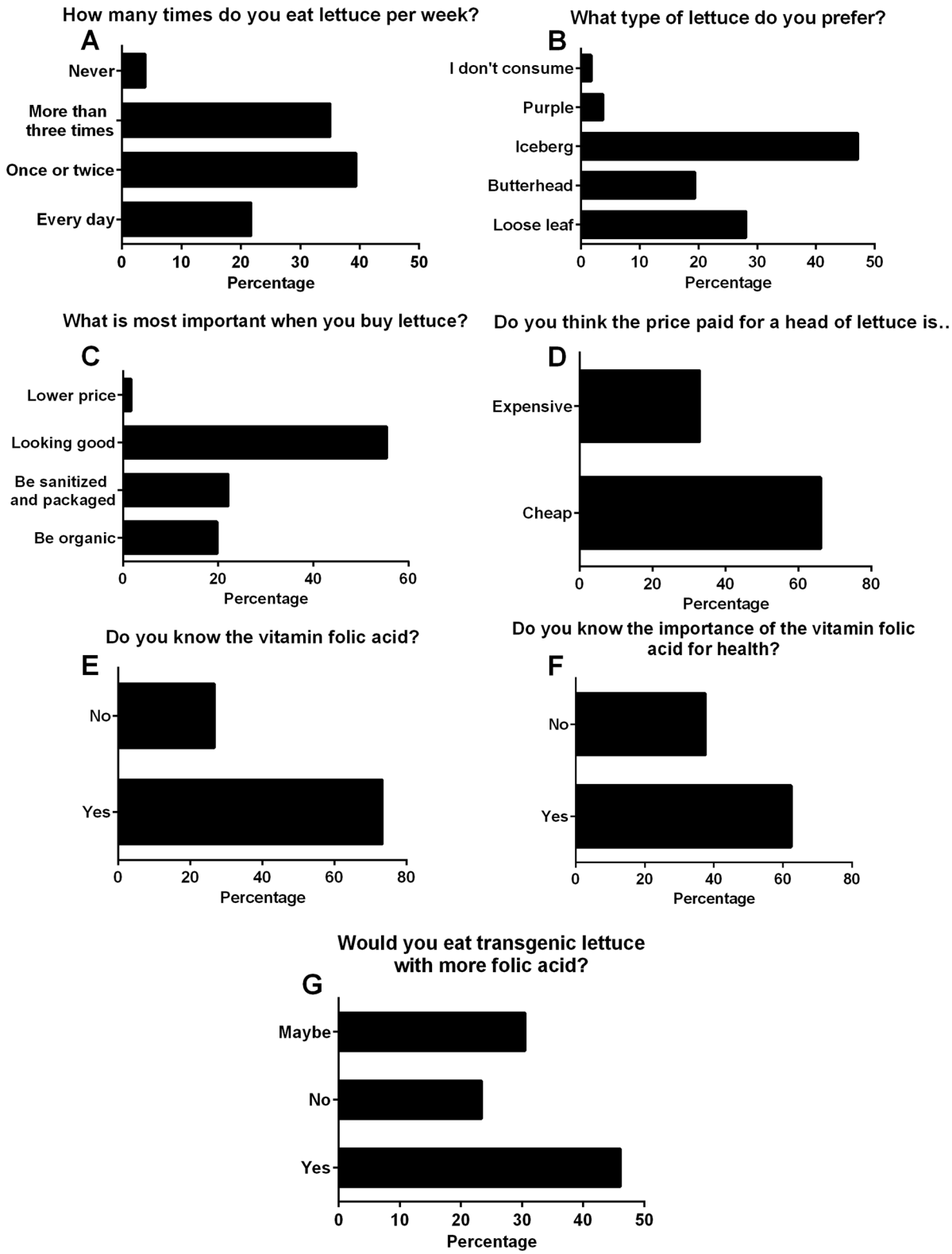

Fig. 3 Histograms showing the response percentages to possible choices for seven questions in the survey

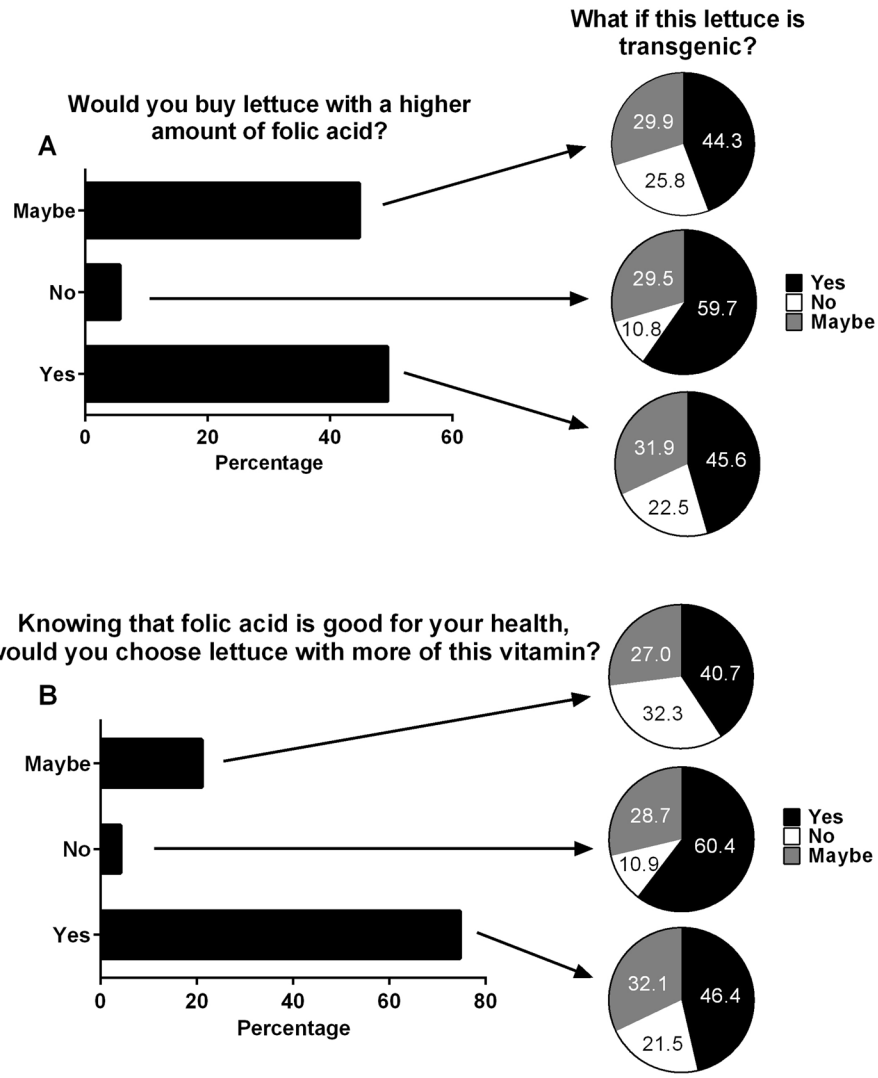

Fig. 4 Histograms showing the response percentages to questions related to acceptance of biofortified lettuce **A**, compared to the response when respondents are informed that folic acid is good for health **B**. Parts-of-whole graphs show the response percentage of respondents who would maintain or not the previous answers if they are informed that the biofortified lettuce is transgenic

and agriculture who argue that GM crops can improve yields, reduce pesticide use and production costs, and address issues like malnutrition through biofortification. Many consumers are skeptical of GM foods due to concerns about their safety for human consumption (Hunt & Wald 2020). Some worry about potential long-term health effects, allergenicity, and unintended consequences of genetic modifications. The organic food movement and the promotion of non-GMO products have gained momentum in response to concerns about GM foods. According to Brazilian law, organic production cannot be carried out with GM crops. However, there was no correlation between people who would choose organic products and those that would refuse to consume transgenic lettuce plants. This shows that there is a disconnection between the regulation for the organic production system and consumers, making room for the consumption of GM lettuce in the near future.

Public perception of GM foods is complex and can evolve over time, as new information becomes available and as consumers and policymakers grapple with the benefits and risks associated with this technology. Public education, transparency, and balanced discussions about the science and safety of GM foods play important roles in shaping public opinion and influencing regulatory decisions. Biofortification can have positive economic and social impacts by reducing healthcare costs associated with nutrient deficiencies. Additionally, it may reduce the need for

expensive nutrient supplementation programs (Ofori et al. 2022).

In Brazil, since the end of the last century, GM crops have been the target of campaigns against the application of genetic engineering in agriculture (Caradus 2023). This campaign produced weekly bulletins widely disseminated over the internet, mainly among upper-middle-class consumers in large cities. These publications bring warnings about the supposed dangers of GMOs for the environment, human and animal health, and the economy. Santos et al. (2023) investigated whether a cultivar of transgenic beans developed by Embrapa, in Brazil, has the potential for adoption in the producer and consumer markets. Through semi-structured interviews, data were collected from non-probabilistic sampling in the state of Goiás, Brazil. The results indicate that producers are prone to planting the transgenic bean. Among consumers, 79% would eat transgenic beans, while 21% would not.

In this work, it is interesting that the majority of respondents said they are willing to consume a GM lettuce if it is biofortified with folic acid. The proportion of people who would eat GM biofortified lettuce is higher in the Midwest region. Perhaps this is a reflection of the fact that this is an agricultural region, where GM crops are mostly grown, such as cotton, corn, soybeans and beans (Klein & Luna 2023). It is interesting to note that most people know about folic acid and its importance, perhaps because of the media and propaganda that recommend it for pregnant women. In fact, since 2002 Brazil has implemented mandatory fortification of wheat and maize flours with folic acid, as a public health strategy aiming to ensure an adequate intake of folic acid among women of childbearing age and preventing neural tube defects in newborns.

Most of the respondents are highly educated individuals. The large majority have a university degree, at least (43.5%), whereas just 19.2% of the general Brazilian population has completed college/university (https://censo2022.ibge.gov.br). In India, a survey with university students revealed a correlation between their knowledge and attitudes about GM foods. Most of the participants agreed to have read about GM foods and defined it correctly. It was observed that attitudes in favor of GM crops were related to higher knowledge scores (Rathod and Hedaoo 2022). A survey by Cui and Shoemaker (2018) reported that 11.9, 41.4, and 46.7% of respondents had a positive, neutral, or negative view on GM food, respectively. A minority of respondents (11.7%) claimed they understood the basic principles of this technology. Stanton et al (2021) used a survey with 500 U.S. participants to verify the extent to which government information influences and changes consumer attitudes. Once consumers were "forced" to read a trusted scientific statement on the safety of GMOs, their concerns about health (involving the possibility of developing cancer) decreased significantly. In the present study, the process to generate the data presented here involved a "snowball" sampling method (Parker et al. 2019). In this process, it is difficult to control the demographic distribution in our sample. Consequently, there were some concentrations in terms of respondents. However, is interesting to observe that highly educated individuals tend to have more knowledge about genetic engineering, biofortification and the importance of vitamins, such as folic acid. In addition, this group can act as opinion leaders. Regarding age groups, our survey mirrors the Brazilian population spread (Pearson correlation $r = 0.84$; $p = 0.00006$), with respondents concentrated between 31 and 65. Nevertheless, "snowball" sampling is particularly useful when it is difficult to access a population directly, as occurs in a large country like Brazil. In addition, it is cost-effective compared to other sampling methods, since participants are recruited through existing networks, which makes them more willing to participate in a study if they are referred by someone they know and trust.

In conclusion, this research demonstrated that if there is an explanation of the advantages in relation to the use of biotechnology, as provided in this study, in this case enrichment with folic acid, acceptance may increase. Therefore, it is recommended that the advantages of biotechnology be publicized and popularized.

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Author contributions TC, MP and FA conceived and conducted the study, analyzed the results, drafted and contributed to the final editing of the manuscript. IN and LQ analyzed the results, drafted and contributed to the final editing of the manuscript. All authors read and approved the final manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

Human or animal rights This article does not contain animal studies. This article had the participation of humans, who participated voluntarily and were informed that data would be anonymously obtained and analyzed.

References

Ahmed ZFR, Alnuaimi AKH, Askri A, Tzortzakis N (2021) Evaluation of Lettuce (Lactuca sativa L) production under hydroponic system: nutrient solution derived from fish waste vs. Inorganic Nutrient Solution. Horticulturae 9(7):292. https://doi.org/10.3390/horticulturae709029

Aliev RI, Kurbanova MN (2022) Prospects for the development of biotechnology: New directions, distribution and application. AIP Conf Proc 2390(1):030001. https://doi.org/10.1063/5.0075804

Bailey LB, Stover PJ, McNulty H, Fenech MF, Gregory JF III, Mills JL, Pfeiffer CM, Fazili Z, Zhang M, Ueland PM, Molloy AM, Caudill MA, Shane B, Berry RJ, Bailey RL, Hausman DB, Raghavan R, Raiten DJ (2015) Biomarkers of nutrition for development-folate review. J Nutr 145(7):1636–1680. https://doi.org/10.3945/jn.114.206599

Birla M, Choudhary C, Singh G, Gupta S, Bhawana VP (2022) The Advent of Nutrigenomics: A Narrative Review with an Emphasis on Psychological Disorders. Prev Nutr Food Sci 27(2):150–164. https://doi.org/10.3746/pnf.2022.27.2.150

Cámara-Martos F, Sevillano-Morales J, Rubio-Pedraza L, Bonilla-Herrera J, de Haro-Bailón A (2021) Comparative Effects of Organic and Conventional Cropping Systems on Trace Elements Contents in Vegetable Brassicaceae: Risk Assessment. Appl Sci 11(2):707. https://doi.org/10.3390/app11020707

Caradus JR (2023) Processes for regulating genetically modified and gene edited plants. GM Crops Food 14(1):1–41. https://doi.org/10.1080/21645698.2023.2252947

Cui K, Shoemaker SP (2018) Public perception of genetically-modified (GM) food: A Nationwide Chinese Consumer Study. Npj Sci Food. 2(1):10. https://doi.org/10.1038/s41538-018-0018-4

da Santos CR, S, Teixeira SM, Cruz JE, Bron PC, (2023). Rev Econ Sociol Rural. https://doi.org/10.1590/1806-9479.2022.250277

FAOSTAT, 2021. www.fao.org/faostat/en/#data/QCL. (Accessed June 06, 2024).

Feng X, Mei Y, Xie P, Xing Z, Wang X, Cui L, Xu R (2023) Serum folic acid: an effective indicator for arteriogenic erectile dysfunction. Front Endocrinol. https://doi.org/10.3389/fendo.2023.1080188

Hunt KP, Wald DM (2020) The role of scientific source credibility and goodwill in public skepticism toward GM foods. Env Com 14(7):971–986. https://doi.org/10.1080/17524032.2020.1725086

ISAAA, 2019. ISAAA Brief 55–2019: Executive Summary. Available Online at: www.isaaa.org/resources/publications/briefs/55/executivesummary/default.asp (accessed June 06, 2024).

Jin S, Li W, Dawson I, Clark B, Chen S, Frewer L (2022a) Consumer responses to genetically modified food in China: the influence of existing general attitudes, affect and perceptions of risks and benefits. Food Qual Prefer. https://doi.org/10.1016/j.foodqual.2022.104543

Jin X, Cheng Z, Yu X, Tao Q, Huang R, Wang S (2022b) Continuous supplementation of folic acid in pregnancy and the risk of perinatal depression–A meta-analysis. J Affect Disord 302:258–272. https://doi.org/10.1016/j.jad.2022.01.080

Kim MJ, Moon Y, Tou JC, Mou B, Waterland NL (2016) Nutritional value, bioactive compounds and health benefits of lettuce (*Lactuca sativa* L.). J Food Compos Anal 49:19–34. https://doi.org/10.1016/j.jfca.2016.03.004

Klein HS, Luna FV (2023) Brazilian crops in the global market: the emergence of brazil as a world agribusiness exporter since 1950. Palgrave Macmillan Cham. https://doi.org/10.1007/978-3-031-38589-6

Li H, Wang X, Zhao H, Wang F, Bao Y, Guo J, Chang S, Wu L, Cheng H, Chen S, Zou J, Cui X, Niswander L, Finnell RH, Wang H, Zhang T (2020) Low folate concentration impacts mismatch repair deficiency in neural tube defects. Epigenomics 12(1):5–18. https://doi.org/10.2217/epi-2019-0279

Magnusson MK, Koivisto Hursti UK (2002) Consumer attitudes towards genetically modified foods. Appetite 39(1):9–24. https://doi.org/10.1006/appe.2002.0486

Medina-Lozano I, Bertolín JR, Díaz A (2021) Nutritional value of commercial and traditional lettuce (Lactuca sativa L) and wild relatives: Vitamin C and anthocyanin content. Food Chem 359:129864. https://doi.org/10.1016/j.foodchem.2021.129864

Mitchell LE (2005) Epidemiology of neural tube defects. Am J Med Gen 135:88–94. https://doi.org/10.1002/ajmg.c.30057

Munaweera TIK, Jayawardana NU, Rajaratnam R, Dissanayake N (2022) Modern plant biotechnology as a strategy in addressing climate change and attaining food security. Agric Food Secur 11(1):1–28. https://doi.org/10.1186/s40066-022-00369-2

Nascimento CP, Cipriano TM, Aragão FJL (2022) Natural variation of folate content in cowpea (*Vigna unguiculata*) germplasm and its correlation with the expression of the GTP cyclohydrolase I coding gene. J Food Compos Anal 107:104357. https://doi.org/10.1016/j.jfca.2021.104357

Nogueira-de-Almeida CA, Zotarelli-Filho IJ, Nogueira-de-Almeida ME, Souza CG, Kemp VL, Ramos WS (2023) Neuronutrients and Central Nervous System: A Systematic Review. Cent Nerv Syst Agents Med Chem 23(1):1–12. https://doi.org/10.2174/1871524923666221121123937

Nunes ACS, Kalkmann DC, Aragão FJL (2009) Folate biofortification of lettuce by expression of a codon optimized

chicken GTP cyclohydrolase I gene. Transgenic Res 18:661–667. https://doi.org/10.1007/s11248-009-9256-1

Ofori KF, Antoniello S, English MM, Aryee AN (2022) Improving nutrition through biofortification–A systematic review. Front Nut 9:1043655. https://doi.org/10.3389/fnut.2022.1043655

Parker C, Scott S, Geddes A (2019) Snowball sampling. SAGE Research Methods Foundations. https://doi.org/10.4135/9781526421036831710

Rathod D, Hedaoo RP (2022) Assessment of Knowledge and Attitudes on Genetically Modified Foods Among Students Studying Life Sciences. Cureus. https://doi.org/10.7759/cureus.32744

Roche ML, Samson KL, Green TJ, Karakochuk CD, Martinez H (2021) Perspective: Weekly Iron and Folic Acid Supplementation (WIFAS): a critical review and rationale for inclusion in the Essential Medicines List to accelerate anemia and neural tube defects reduction. Adv Nut 12(2):334–342. https://doi.org/10.1093/advances/nmaa169

Shi M, Gu J, Wu H, Rauf A, Emran TB, Khan Z, Mitra S, Aljohani ASM, Alhumaydhi FA, Al-Awthan YS, Bahattab O, Thiruvengadam M, Suleria HAR (2022) Phytochemicals, Nutrition, Metabolism, Bioavailability, and Health Benefits in Lettuce-A Comprehensive Review. Antioxidants (basel) 11(6):1158. https://doi.org/10.3390/antiox11061158

Stanton J, Rezai G, Baglione S (2021) The effect of persuasive/possessing information regarding GMOs on consumer attitudes. Future Foods. https://doi.org/10.1016/j.fufo.2021.100076

Tsiklauri R, Parvanta I, Jijeishvili L, Kherkheulidze M, Kazakhashvili N (2019) Folate Deficiency and Its Impact on NTDs Prevalence in Georgia. Biom J Sci Tech Res 23(1):17156–17161. https://doi.org/10.26717/BJSTR.2019.23.003853

Wang L, Ning S, Zheng W, Guo J, Li Y, Li Y, Chen X, Ben-Gal A, Wei X (2023) Performance analysis of two typical greenhouse lettuce production systems: commercial hydroponic production and traditional soil cultivation. Front Plant Sci 14:1–15. https://doi.org/10.3389/fpls.2023.1165856

Yang X, Gil MI, Yang Q, Tomás-Barberán FA (2022) Bioactive compounds in lettuce: Highlighting the benefits to human health and impacts of preharvest and postharvest practices. Comp Rev Food Sci Food Safety 21:4–45. https://doi.org/10.1111/1541-4337.12877

Zhang T, Liang Z, Lin T, Cohen DJ, Arrieta A, Wang X, Zhang Z (2022) Cost-effectiveness of folic acid therapy for primary prevention of stroke in patients with hypertension. BMC Med 20(1):1–14. https://doi.org/10.1186/s12916-022-02601-z