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COMPREHENSIVE REVIEW

# Revisiting the Nutritional and Health-Promoting Properties of Soy Protein-Based Food Formulations for Infants and Adults

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## ABSTRACT

Soy protein (SP), a high-quality, plant-based protein derived from *Glycine max* (soybean), has gained global prominence as a nutritional staple and a functional ingredient in diverse dietary applications. It not only contains all essential amino acids (AAs), but also its recognition as a complete protein—containing all essential AAs—and its low saturated fat content make SP a valuable component in vegetarian and vegan diets. Despite its growing popularity, the health effects of the SP remain a subject of scientific and public scrutiny, especially in sensitive populations such as infants and older adults. Soy-based infant formulas are commonly used alternatives to cow's milk-based formulas, yet questions persist regarding their safety and the long-term effects of early isoflavone exposure. In adults, SP is investigated for its impact on muscle maintenance, metabolic health, and aging, though individual responses may vary based on age, sex, and metabolic profile. This review aims to critically examine the current evidence on the nutritional value and functionality of SP in infants and adults. We assess the benefits, limitations, and potential health implications of SP across the lifespan. Current evidence supports the safety of soy formulas in term infants, with no adverse neurodevelopmental or endocrine outcomes. In adults, SP consumption is associated with modest lipid-lowering and bone-protective effects, though study heterogeneity remains. Our objective is to provide a nuanced understanding of SP's role in human nutrition and identify areas requiring further scientific inquiry to support informed dietary guidelines and public health policy.

**Abbreviations:** AAP, American Academy of Pediatrics; AAs, amino acids; ADHD, attention-deficit hyperactivity disorder; ANFs, anti-nutritional factors; AnPr, animal-based proteins; ASD, autism spectrum disorder; Cmilk, cow's milk; CMPA, Cmilk protein allergy; CVDs, cardiovascular diseases; CVR, CVD risk; DIAAS, Digestible Indispensable AA Score; EAAs, essential AAs; EFSA, European Food Safety Authority; ERα, estrogen receptor α; ERβ, estrogen receptor β; ESPGHAN, European Society for Pediatric Gastroenterology Hepatology and Nutrition; US FDA, US Food and Drug Administration; FORWARD, Fragile X Online Registry with Accessible Research Database; LDL-C, low-density lipoprotein cholesterol; IARC, International Agency for Research on Cancer; LCAs, life cycle assessments; HDL-C, high-density lipoprotein cholesterol; NTP, National Toxicology Program; OFAs, omega-3 fatty acids; PDCAAS, $P_{Digest}$-corrected AA score; $P_{Digest}$, protein digestibility; PDPs, plant-derived proteins; RTRS, Roundtable on Responsible Soy; SbF, soy-based formulas; SP, soy protein; SPC, SP concentrate; SPI, SP isolate; TNF-α, tumor necrosis factor-alpha.

## 1 | Introduction

Soy protein (SP), derived from the legume *Glycine max* (soybean), has a rich cultural and agricultural history spanning over 2000 years, particularly in East Asia, where soy-based foods such as tofu, miso, tempeh, natto, and soy milk have been integral components of traditional diets (Baraibar and Deutsch 2023). However, it was not until the 20th century that SP gained global recognition, propelled by advances in food processing technologies that enabled its extraction and incorporation into a wide array of food products, including meat analogs, dairy alternatives, protein bars, nutritional supplements, and infant formulas. The processing of soybeans into protein-rich products was initially motivated by their high protein content and versatility, cost-effectiveness, economic factors, agricultural sustainability with nitrogen fixation, food security concerns, oil production, cultural food practices, shelf stability, and storage advantages (Qin et al. 2022; Raita et al. 2025; Sui et al. 2021; van den Berg et al. 2022; Zhang et al. 2021). Advancements in food technology facilitated the extraction and concentration of SP, giving rise to SP isolate (SPI) and SP concentrate (SPC), which became widely utilized in both infant and adult nutrition and the broader food industry (Zhao et al. 2023).

In recent decades, SP has experienced a surge in global popularity, fueled by multiple converging factors: the rise of plant-based diets, growing awareness of the environmental impacts of animal agriculture, and increased demand for sustainable and ethically produced food sources (Qin et al. 2022; Thrane et al. 2024). As a result, SP is now a foundational ingredient in many food formulations (Yan et al. 2024). It is also a key component in infant soy-based formulas (SbF), providing an alternative to cow's milk (Cmilk)-based options for infants with lactose intolerance, Cmilk protein allergy (CMPA), or families adhering to vegetarian or vegan dietary patterns (Ashaolu et al. 2017, 2019; Verduci et al. 2020; Ashaolu and Suttikhana 2023). The importance of SP in human nutrition lies in its unique composition. It is one of the few plant-derived proteins (PDPs) considered "complete," as it contains many amino acids (AAs), including all nine essential AAs (EAAs) in proportions suitable for human health (Ashaolu et al. 2019). Furthermore, SP is low in saturated fat, free of dietary cholesterol, and rich in bioactive compounds (bioactives), for example, isoflavones, which possess antioxidant and estrogen-like properties. These characteristics have positioned SP not only as a functional ingredient in food formulation but also as a potential contributor to disease prevention, including cardiovascular disease (CVD), osteoporosis, and certain cancers (Kim 2021). For vegetarians and vegans, populations who may have limited access to high-quality protein sources, SP plays a crucial role in meeting daily protein needs and supporting physiological functions throughout life.

Nevertheless, incorporation of SP into diets across different age groups remains an area of scientific and public debate. In infants, concerns have been raised regarding the long-term safety of SbF, particularly related to isoflavone exposure and endocrine development (Testa et al. 2018). The concerns focus on potential effects of phytoestrogens on hormonal development, as well as the bioavailability of key nutrients, for example, iron and zinc (Vandenplas et al. 2021). In adults, the effectiveness and functional roles of SP continue to be investigated in the context of muscle maintenance, metabolic health, hormonal regulation, and aging (Krishnan et al. 2022; Zheng et al. 2022). Although SP is widely consumed for its muscle-building and cardioprotective effects, questions remain about its digestibility, allergenicity, and comparative effectiveness against other high-quality proteins (van den Berg et al. 2022). Emerging evidence suggests that age, sex, health status, and gut microbiota composition may influence how individuals metabolize and respond to SP and its bioactives (Tamura et al. 2019; Ashaolu 2020; Deng et al. 2022). Furthermore, functional properties of SP—such as its emulsification, gelation, and water-binding capacities—play a crucial role in food applications, influencing both nutritional quality and consumer acceptance (Huang et al. 2023).

Given these considerations, this review aims to comprehensively assess the nutritional benefits and health-promoting properties of SP across the lifespan, with a particular focus on infants and adults. We evaluate the role of SP in infant nutrition, examining its adequacy as a protein source in SbF, potential health implications, and comparisons with breast milk and Cmilk-based alternatives; analyze the benefits and limitations of SP in adult diets, focusing on its contributions to muscle protein synthesis, metabolic health, and chronic disease prevention; and discuss the technological and functional aspects of SP in food formulations, addressing how processing methods influence its nutritional quality and sensory properties.

## 2 | Methods

To identify relevant literature, we conducted a comprehensive search of the PubMed, Scopus, Google Scholar, and Web of Science databases for articles published between January 2000 and March 2025. Search terms included combinations of "SP," "soy formula," "isoflavones," "plant-based protein," "infants," "adults," "health outcomes," "lipids," "bone health," and "safety." We included peer-reviewed human studies, systematic reviews, and meta-analyses published in English. Studies were selected based on relevance to the nutritional and functional roles of SP across the lifespan. Priority was given to studies with clearly defined outcomes, adequate sample sizes ($n \geq 30$), and appropriate control groups. Animal studies, in vitro experiments, and non-peer-reviewed sources were excluded.

## 3 | Nutritional Composition of SPs

SP has emerged as one of the most nutritionally significant PDPs due to its high-quality AA profile, functional versatility, and unique bioactives (Table 1). SP products vary in macronutrient content depending on their degree of processing. For instance, SPI is the most refined form, and it contains the highest protein (80%–90%), making it comparable to animal-based proteins (AnPr) based on protein content (Zheng et al. 2022). Although whole soybeans and soy flour contain notable amounts of polyunsaturated fats (including omega-3 $\alpha$-linolenic acid), processing significantly reduces fat content in SPI and SPC (Verfaillie et al. 2023). SP contains carbohydrates and fiber. Soy flour retains the highest fiber content, primarily insoluble, which is largely removed in SPI. However, SPI may still contain small amounts

**TABLE 1** | Nutritional composition of soy protein isolate (per 100 g).

| Nutrient | Amount | Notes |
|---|---|---|
| **Energy** | 335–370 kcal | Varies slightly by manufacturer and processing |
| **Protein** | 85–90 g | High-quality, complete protein (PDCAAS ∼1.0) |
| **Total fat** | 0.5–1.5 g | Very low fat content |
| –Saturated fat | <0.2 g | Minimal |
| –Unsaturated fat | ∼0.3–1.3 g | Includes linoleic acid (omega-6) |
| **Carbohydrates** | 1–3 g | Mostly fiber, negligible sugar |
| –Dietary fiber | 0.5–2 g | Insoluble |
| –Sugars | <0.5 g | Trace amounts |
| **Cholesterol** | 0 mg | Cholesterol-free (plant-based) |
| **Calcium** | 80–200 mg | Variable depending on product |
| **Iron** | 6–15 mg | Nonheme iron |
| **Magnesium** | 60–100 mg | Muscle and nerve function |
| **Phosphorus** | 600–800 mg | Bone and cellular metabolism support |
| **Potassium** | 50–150 mg | Regulates fluid and nerve function |
| **Zinc** | 1–3 mg | Essential for immune health |
| **Sodium** | 100–1000 mg | Processing-dependent |
| **Isoflavones** | 50–150 mg | Genistein, daidzein, and glycitein (phytoestrogens) |

Abbreviation: PDCAAS, $P_{Digest}$-corrected AA score.
*Source:* Messina (2010), US Department of Agriculture (USDA) (2015).

**TABLE 2** | Comparative amino acid profiles (mg/g protein).

| Amino acid | Soy protein isolate | Whole egg | Whey protein | FAO requirement |
|---|---|---|---|---|
| Histidine | 26 | 22 | 16 | 15 |
| Isoleucine | 49 | 54 | 54 | 30 |
| Leucine | 82 | 86 | 89 | 59 |
| Lysine | 63 | 70 | 89 | 45 |
| Methionine + cysteine | 26 | 57 | 42 | 22 |
| Phenylalanine + tyrosine | 84 | 93 | 56 | 38 |
| Threonine | 38 | 47 | 65 | 23 |
| Tryptophan | 14 | 17 | 17 | 6 |
| Valine | 50 | 66 | 48 | 39 |

*Source:* Friedman and Brandon (2001), Messina (2016), Soy Nutrition Institute (2025).

of oligosaccharides (e.g., stachyose and raffinose), which can contribute to gut microbiota fermentation (Miao et al. 2024).

SP is one of the few PDPs classified as a complete protein, containing all nine EAAs in an adequate amount (Ashaolu 2020). It is particularly rich in lysine, an EAA often limited in cereals, making it an excellent complement to grain-based diets. However, it is marginally lower in methionine (Table 2) compared to AnPr (e.g., whey and casein), though this is easily mitigated by dietary diversity (e.g., pairing with grains or nuts) (Zhang et al. 2022; Fatkhullaev et al. 2023). With regards to protein digestibility ($P_{Digest}$), SPI has a $P_{Digest}$-corrected AA score (PDCAAS) = 1.0 (the highest possible score) and a Digestible Indispensable AA Score (DIAAS) = 84–92, indicating high bioavailability (Ahsan et al. 2018; Jiménez-Munoz et al. 2021; Zhang, Li, et al. 2023). The PDCAAS and the DIAAS are standardized methods used to evaluate protein quality based on human AA requirements and digestibility. A PDCAAS of 1.0 (the highest possible score) indicates that the protein provides all EAAs in adequate amounts and is highly digestible. DIAAS, a more recent method, offers a refined assessment by considering individual AA digestibility at the end of the small intestine. The SP consistently scores highly on both scales, confirming its status as a high-quality PDP (Ahsan et al. 2018; Jiménez-Munoz et al. 2021). Soy isoflavones, for example, genistein and daidzein, are naturally occurring plant compounds classified as phytoestrogens. They can bind to estrogen receptors in the body, mimicking or modulating the effects of estrogen. This estrogenic activity is believed to underlie many of soy's potential health benefits, including support for bone health, cardiovascular function, and relief of menopausal symptoms. However, their effects are generally much weaker than endogenous estrogen and vary depending on individual metabolism and hormonal status (Kim 2021).

SP also contains significant levels of essential minerals, though bioavailability can be affected by phytates, which chelate divalent cations like iron and zinc (Uddin et al. 2016). SPI and SPC have iron contents of 16 and 10 mg/100 g, respectively (Hackl et al. 2025). The isoflavones in SP, including genistein, daidzein, and glycitein, exhibit phytoestrogenic activity, with potential benefits for cardiovascular health, bone density, and menopausal symptoms (Kim 2021). The saponin contents are associated with anti-inflammatory, antioxidative, immune-modulatory, and anticancer properties (White and Dilger 2024). Compared with other proteins, SP's sustainability and hypoallergenicity when hydrolyzed make it preferable for infants with Cmilk allergy (Ashaolu et al. 2019; Deglaire et al. 2023). Cmilk is considered unsustainable due to its significant environmental impact, primarily from greenhouse gas emissions, high water consumption, and land use. The dairy industry's footprint is notably larger than that of plant-based milk alternatives. Nonetheless, some SP and other food manufacturers are committed to using organic and non-GMO ingredients from sustainable farming practices. However, SP's lower leucine content compared to whey may slightly reduce its anabolic potential for muscle synthesis (Van Vliet et al. 2015).

Various processing techniques significantly alter the nutritional profile of SP, with distinct effects on protein quality, carbohydrate content, and mineral bioavailability. Heat processing, such as toasting or extrusion, improves protein digestibility ($P_{Digest}$) by denaturing trypsin inhibitors and lectins; however, excessive heat can trigger Maillard reactions, reducing the bioavailability of EAAs like lysine (Takács et al. 2022; van den Berg et al. 2022; Ke et al. 2024). Fermentation, used in producing tempeh and miso, enhances protein digestibility (reaching up to 92.7% for tofu compared to 65.3% for steamed beans) and degrades flatulence-causing oligosaccharides (Qin et al. 2022). Fermentation also increases isoflavone aglycone content and significantly improves mineral bioavailability by degrading phytate complexes that would otherwise bind to minerals like iron and zinc in the gut (Harahap et al. 2025). Conversely, isolation and concentration processes, such as those used for SPI, effectively remove indigestible carbohydrates and antinutritional factors (ANFs), resulting in a high protein content with digestibility of 93%–97% (van den Berg et al. 2022). Alkalization, often employed in SPI production, adjusts pH to remove oligosaccharides but may concurrently alter protein structure (Harahap et al. 2025).

## 4 | Health Benefits of SPs

### 4.1 | In Infants

Infancy is a significant period of rapid growth needing optimized nutrition for adequate organ development and optimal health. To maintain this, essential nutrients, including carbohydrates, proteins, fats, vitamins, and minerals, should be provided to them in a balanced feeding. Breastfeeding can supply all the required nutrients. Besides, the benefits of additional protein intake in infancy with supplemented infant formulas have become widely recognized (Vandenplas et al. 2021). For infants with particular nutritional demands to support rapid growth and development, SbF are essential because they provide a complete protein source that satisfies all of their developmental requirements. These formulas, which contain important AAs, fortified vitamins, and minerals similar to those found in conventional formulas made from Cmilk, offer a nutritional profile that is carefully balanced and intended to assist newborn growth. SbF undergo extensive evaluation for nutritional adequacy, ensuring they adhere to stringent regulations implemented by regulatory agencies such as the US Food and Drug Administration (FDA) (Messina et al. 2017). Their hypoallergenic characteristics are one of the main benefits of infant SbF, which makes them an excellent alternative for babies who are lactose intolerant or allergic to dairy. The macronutrient profiles needed for ideal infant growth are matched in SbF, which are nutritionally designed to enhance both cognitive and physical development. Extensive nutritional evaluations and quality control procedures are required by regulatory agencies for infant SbF as well as all other infant formulas. These guidelines ensure that the formulas include an adequate amount of the vitamins, minerals, proteins, fats, and carbohydrates needed for an infant's diet (Ashaolu 2020; Ashaolu et al. 2023).

Current medical guidelines support the use of soy-based infant formulas as safe and suitable infant nutrition. The American Academy of Pediatrics (AAP) suggests SbF as a nutritionally appropriate alternative for term infants who cannot tolerate Cmilk formula; that is, infants with galactosemia, infantile hereditary lactase deficiency, or optional for families with vegan dietary preferences (Fuchs et al. 2023). Similarly, in their guideline statements, the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) stated that SbF may be an acceptable alternative based on medical need; however, breastfeeding remains the best option for infant feeding (ESPGHAN Guidelines 2025). Infant SbF are regulated by the US FDA as infant formulas meeting all nutritional requirements as Cmilk formula, ensuring the formulas provide acceptable macronutrient amounts and micronutrients to promote normal growth and development. Due to decades of safety assessment regulations, this interpretative effectiveness creates a basis for evaluating new research on SbF outcomes on hundreds of thousands of infants (FDA 2025). International evidence is also consistent regarding this safety assessment. For example, Health Canada, the Australian Department of Health, and regulations from Asia-Pacific regions have drawn similar conclusions regarding SbF safety (Australian Government Department of Health and Aged Care 2025; Government of Canada 2025). East Asian countries with traditionally high soy consumption continue to reference and include soy-based products within infant feeding as an acceptable option in a culturally appropriate manner (OECD 2022).

Personalized dietary recommendations and routine pediatric reviews are advised by medical specialists to track each infant's growth and metabolic reactions, taking into account potential changes in protein bioavailability and individual metabolic characteristics (Vandenplas et al. 2021). Although SbF have several nutritional advantages, the presence of phytoestrogens and the requirement for appropriate vitamin supplementation are possible factors to take into account (Leung et al. 2009). The best dietary plan should be decided by parents and medical professionals working together, considering the developmental demands, possible allergies, and specific nutritional needs of each infant (Lee and Neio Demirci 2023; Lee and Taştemir 2023). Various health impacts of SP on infants are presented in Table 3.

For infants, SbF are considered safe and nutritionally adequate for term infants who cannot consume Cmilk-based formulas, including those with lactose intolerance or galactosemia. Regulatory bodies, such as AAP and the European Food Safety Authority (EFSA), support their use, though they are not recommended for preterm infants due to limited data. Typical isoflavone exposure from SbF is estimated at 6–11 mg/kg/day, which has not been associated with adverse endocrine or neurodevelopmental outcomes in long-term studies (Bhatia and Greer 2008). For adults, moderate SP intake, ranging from 15 to 25 g/day, is associated with health benefits, including modest reductions in low-density lipoprotein cholesterol (LDL-C), improved arterial flexibility, and potential bone-protective effects. The US FDA permits a health claim for SP and heart disease, recommending 25 g/day as part of a diet low in saturated fat and cholesterol (Bhatia and Greer 2008). SP is widely used in food processing due to its functional properties, including emulsification, gelation, water-holding capacity, and texturization. It is a key ingredient in meat analogs, dairy alternatives, protein bars, and bakery products. Different forms, such as soy flour, SPC, and SPI, are selected on the basis of desired texture, protein content, and processing needs. Advances in extrusion and fermentation technologies have further enhanced the sensory and nutritional profiles of soy-based foods (Jang and Lee 2024).

#### 4.1.1 | Central Nervous System

Numerous studies involving electrophysiological assessments in infants given various types of milk, including infant SbF, have been carried out to determine whether diet may have an impact on neurologic development because human brain electrical or electroencephalographic activity has been connected to brain maturation as well as behavioral and cognitive function. Ha et al. (2021) examined the impact of consuming infant SbF between 9 and 12 months after birth on the development of epilepsy and neurodevelopmental difficulties, and the level of development was examined. Accordingly, 11,535 (7.5%) of the 153,841 eligible participants were given SbF, whereas 142,864 (92.5%) were given Cmilk formula. The results showed that there was no significant difference between the two groups according to a predetermined analysis utilizing different criteria for epilepsy. Similarly, there were no significant correlations between SbF and developmental delays, attention-deficit hyperactivity disorder (ADHD), or autism spectrum disorder (ASD) (Ha et al. 2021). Moreover, through a retrospective case-control survey study of participants with Fragile X syndrome enrolled in the Fragile X Online Registry with Accessible Research Database (FORWARD), the potential associations between the consumption of SbF during infancy and disease complications in individuals with Fragile X syndrome were evaluated by Westmark et al. (2020), while accounting for potential confounding factors. The percentage of the study population using infant SbF was 25%. The complications of autism, digestive disorders, and allergies were found to be significantly correlated with the use of baby SbF. Particularly, among those who reported using infant SbF, the incidence of autism was 1.5 times higher, digestive disorders were 1.9 times higher, and allergies were 1.7 times higher. Digestive disorders were the primary driver behind the use of baby SbF. The typical age at which seizures and allergies started was a long time after the infant had received SbF. The result exhibited that giving baby SbF to children at a young age is linked to the emergence of many illness complications in Fragile X syndrome (Westmark et al. 2020).

Bellando et al. (2020) investigated the influence of the main infant food regimens on the growth of electrical activity in the brain throughout infancy; 120 full-term, healthy infants were either breastfed or given milk formula or SbF for the first 6 months of their infant years. Resting brain electrical or electroencephalographic activity was recorded from 124 electrode sites on the scalp of the same infants using a high-density array net during calm wakefulness, when the infants were 3, 6, 9, and 12 months old. There were significant differences in diet across frequency bands, including time-related effects. Although formula-fed groups usually exhibit similar brain electrical activity development during infancy, breastfed infants vary from those fed either milk formula or SbF. Childhood cognition and language development were evaluated during the first 5 years of life in infants fed breast milk, Cmilk formula, or SbF. The participants were 504 eligible infants between 2 and 12 months old. The infants, who weighed between 2.7 and 4.1 kg at birth, were >37 weeks and had not received any known medical diagnoses or drugs that may have impacted their growth or development. From age 36 to 60 months, children who were breastfed, formula-fed with Cmilk, or formula-fed with SP had longitudinal neurodevelopment assessments. Differences by sex were also investigated. The results exhibited that between the ages of 3 and 5, breastfeeding was linked to minor, statistically significant variations in verbal ability, expressive communication, and auditory comprehension. The latter may have a sexual dimorphic impact. However, these distinctions are still minor and could not have any clinical significance. Besides, there were no notable differences between Cmilk-fed and SP-fed (Bellando et al. 2020).

The interaction between infant SbF and seizure occurrence was investigated in children with autism in another study (Westmark 2014). Information from 1949 autistic children's medical records was taken from the Simons Foundation Autism Research Initiative Simplex Collection. The results of the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule tests were used to diagnose autism in the autism birth cohort. Records on infant formula consumption, seizure incidence, seizure type, and IQ were all included in the database. Overall, 17.5% of the research participants used SbF. Intelligence level, age at which seizures began, infantile spasms, atonic, generalized tonic–clonic, absence, and complex partial seizures were among the other outcomes for which no statistically significant correlations were discovered. The consumption of baby SbF may be linked to both male and female autistic children being diagnosed with epilepsy and experiencing febrile seizures

**TABLE 3** | Studies showing the impacts of soy-based formula (SbF) on health status of infants.

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | Reference |
|---|---|---|---|---|---|
| **Central nervous system** | | | | | |
| Epilepsy, ADHD, and ASD | The impact of consuming infant SbF between 9 and 12 months after birth on the development of epilepsy, neurodevelopmental difficulties, and level of development | Infants between 9 and 12 months old | A retrospective, national, population-based observational cohort study with 11,535 (7.5%) of the 153,841 eligible participants given SbF, whereas 142,864 (92.5%) were given cow's milk (Cmilk) formula | No significant difference between the two groups according to a predetermined analysis utilizing different criteria of epilepsy. There were no significant correlations between SbF and developmental delays, ADHD, or ASD | Ha et al. (2021) |
| Fragile X syndrome | The potential associations between the consumption of SbF during infancy and disease complications in individuals with FXS were evaluated while accounting for potential/confounding factors | 122 enrolled participants with a seizure history and 448 participants with non-seizure cases as controls | Through a retrospective case-control survey study of participants with Fragile X syndrome enrolled in the Fragile X Online Registry with Accessible Research Database | The incidence of autism was 1.5 times higher, digestive disorders were 1.9 times higher, and allergies were 1.7 times higher. Digestive disorders were the primary driver behind the use of baby SbF. Giving baby SbF to children at a young age is linked to the emergence of many illness complications in Fragile X syndrome | Westmark et al. (2020) |
| Brain maturation and behavioral and cognitive function | The influence of the main infant food regimens was investigated on the growth of electrical activity in the brain throughout infancy | A total of 120 full-term, healthy infants were either breastfed or given Cmilk formula or SbF for the first 6 months of their infant years | Resting brain electrical or electroencephalographic activity was recorded from 124 electrode sites on the scalp of the same infant using a high-density array net during calm wakefulness, when the infants were 3, 6, 9, and 12 months old | Although formula-fed groups usually exhibit similar brain electrical activity development during infancy, breastfed infants vary from those fed either Cmilk formula or SbF. These differences in electroencephalographic activity displayed how nutrition affects the structure and function of the brain, which may place babies on distinct neurodevelopmental paths that will influence their cognitive and brain function development | Jing et al. (2010) |

(Continues)

TABLE 3 | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | Reference |
|---|---|---|---|---|---|
| Cognition and language development | Development of childhood cognition and language was evaluated during the first 5 years of life in infants fed breast milk, Cmilk formula, or SbF | 504 eligible infants were between 2 and 12 months old. The infants weighed between 2.7 and 4.1 kg at birth and were >37 weeks | From age 36 to 60 months, children who were breastfed, formula-fed with Cmilk, or SP had longitudinal neurodevelopment assessments. Differences by sex were also investigated | Between the ages of 3 and 5, breastfeeding was linked to minor, statistically significant variations in verbal ability, expressive communication, and auditory comprehension. The latter may have a sexual dimorphic impact. However, these distinctions are still minor and could not have any clinical significance. Besides, there were no notable differences between Cmilk-fed and SP fed | Bellando et al. (2020) |
| Seizure and autism | The interaction between infant SbF and seizure occurrence was investigated in children with autism | Of the 1949 autistic children in the population, 86.6% were male, and 13.4% were female | Children's medical records were taken from the Simons Foundation Autism Research Initiative Simplex Collection. The results of the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule tests were used to diagnose autism in the autism birth cohort. 17.5% of the research participants used SbF | Intelligence level, age at which seizures began, infantile spasms, atonic, generalized tonic–clonic, absence, and complex partial seizures were among the other outcomes for which no statistically significant correlations were discovered. The consumption of baby SbF may be linked to both male and female autistic children being diagnosed with epilepsy and experiencing febrile seizures | Westmark (2014) |
| Anthropometric growth, bone health, immunity, cognition, and reproductive and endocrine functions | The safety of infant SbF was examined in children for anthropometric development, immunity, bone health, cognition, and reproductive and endocrine functioning | Infants or children under the age of 18, regardless of their clinical condition, language, or place of origin | The current evaluation included cross-sectional, case-control, cohort, or clinical studies for children who were fed infant SbF, Cmilk-based formulas, or human milk | Current infant SbF are safe, evidence-based choices for feeding infants and children with nutritional requirements. Children fed with these three types of milk have equivalent growth, bone health, metabolic, reproductive, endocrine, immunological, and neurological characteristics | Vandenplas et al. (2014) |
| Developmental status in mental, motor, and language | The mental, motor, and linguistic development of infants was investigated | 391 healthy newborns were breastfed, milk-based formula-fed, or SbF-fed throughout their first year of life | A longitudinal assessment was conducted at 3, 6, 9, and 12 months of age. The Bayley Scales of Infant Development and the Preschool Language Scale-3 were used to assess development | No significant difference between the milk-fed and soy-fed groups, and all developmental test results fell within acceptable standard norms. Additionally, breastfed newborns had a little intellectual growth advantage over formula-fed infants | Andres et al. (2012) |

(Continues)

**TABLE 3** | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | Reference |
|---|---|---|---|---|---|
| **Immune system** | | | | | |
| Intestinal microbiota | The influence of soy-based milk consumption in the infant intestinal ecosystem was determined | 12 infants aged from 3 to 8 months, including 8 males and 4 females, were selected | Soymilk was used to substitute the formula made from Cmilk for twelve infants. The infant intestinal microbial composition was examined both before and after the change in diet | The findings reveal that SbF feeding has no effect on infants' gastrointestinal (GI) microbes or the population of intestinal bifidobacteria | Piacentini et al. (2010) |
| GI tolerance and hydration status | Assessing the relative GI tolerance of healthy infants provided the two experimental powdered SbF containing supplemental fructooligosaccharides in comparison to a commercial control SbF usage was studied | Infants were singleton, healthy-term infants with gestational ages of 37–42 weeks, from 0 to 8 days of age, with a birth weight >2.5 kg | A multicenter, parallel, randomized, double-blind feeding research was carried out. Healthy-term newborns were recruited for the trial, randomly allocated to one of three study formulas, and given only the designated study formula from birth to 35 days | The study completion rates, growth, stool consistency and frequency, formula intake, vomit, and safety variables were not significantly different. Over the first 35 days of life, infants fed SbF supplemented with short-chain fructooligosaccharides and mixed carotenoids, with or without sucrose, demonstrated good tolerance and hydration equivalent to the control SbF that was considered safe | Lasekan et al. (2015) |
| Vaccine responses and morbidity | Infants fed SbF with and without additional nucleotides for a year were assessed for their immunological state and morbidity | Healthy term 267 infants with gestational ages of 37–42 weeks from nine sites were enrolled from birth to 8 days of age | In a 12-month masked feeding process, infants were randomized to groups that received SbF with or without additional nucleotides. Concurrent enrollment included a nonrandomized human milk cohort. At 2, 4, and 6 months, the recommended vaccinations were provided. At 6, 7, and 12 months, antibody responses to the poliovirus, tetanus, diphtheria, and *Haemophilus influenzae* Type B vaccinations were used to evaluate the immune system | Infants fed soy milk supplemented with and without nucleotides did not exhibit any significant differences in their responses. Nevertheless, compared to infants fed human milk or formula, those fed nucleotide-supplemented soy had greater levels of antibodies against *H. influenzae* Type B at 7 and 12 months. At 12 months, infants fed human milk disclosed greater levels of poliovirus-neutralizing antibodies than infants fed soy milk. As indicated by antibody responses to childhood vaccinations, infants fed SbF demonstrate normal immunological development | Ostrom et al. (2002) |

(Continues)

**TABLE 3** | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | Reference |
|---|---|---|---|---|---|
| Immune cell status | The populations of immune cells were examined in infants fed SbF with and without additional nucleotides | Healthy term 267 infants were enrolled from birth to 8 days of age | Three-color flow cytometry was used to analyze 32 immune cell types. Blood samples were taken at 6, 7, and 12 months. Cellular markers that focus on the development and activation of B, T, and NK cells were selected to evaluate the overall immunological state of infants | Infants fed SbF indicated immune cell status comparable to infants fed human milk, which is compatible with the normal development of the immune system. Although individual immune cell populations were not significantly influenced by the addition of nucleotides to SbF, it did seem to raise the population of T cells and reduce that of NK cells | Cordle et al. (2002) |
| **Reproductive system** | | | | | |
| Reproductive hormones | Vaginal cells from soy-fed infant girls were investigated on alteration of DNA methylation in correlation with SbF exposure | 50 girls between birth and 9 months of age | Vaginal cells with epigenome-wide DNA methylation were examined from four girls fed SbF and six girls fed Cmilk formula. Pyrosequencing for 214 vaginal cell samples is used to monitor the two most differentially methylated locations | The modification of DNA methylation in vaginal cells is found in female infants fed SbF, and this might have been attributed to a reduction in the expression of an estrogen-responsive gene | Harlid et al. (2017) |
| Reproductive hormones | The relationship between the different dietary patterns of male infants with the hormone-responsive tissues and reproductive hormones was assessed | Healthy term 147 male infants | Infants were fed SbF, Cmilk formula, or breast milk in a prospective cohort study. The samples were collected between birth and 28 weeks of age. Mixed-effects regression splines are used to analyze dietary differences in age trends for these results | Infancy exposure to phytoestrogen has no effect on these indicators of early male reproductive development | Chin et al. (2021) |
| Reproductive organ volumes and structural characteristics | The size and anatomical features of the reproductive organs were investigated in 5-year-old children | 101 children (containing 50 boys and 51 girls) aged 5 years old who were breastfed ($n = 35$) or fed Cmilk formula ($n = 32$) or SbF ($n = 34$) as infants | Volumes and features of the breast bud, uterus, ovaries, prostate, and testes were evaluated by sonography under the beginnings of a long-term cohort study | Early infant nutrition did not impact the volumes and anatomical features of the reproductive organs in this cohort of 5-year-olds | Andres et al. (2015) |
| **Thyroid gland** | | | | | |
| Goiter and overt hypothyroidism | SbF consumption may negatively impact thyroid function in people who are iodine deficient or have subclinical hypothyroidism | A boy toddler at the age of 22 months, who had previously been diagnosed with a Cmilk allergy, appeared at the clinic with significant goiter and overt hypothyroidism | The boy had been following a strict soy milk-based diet since he was 12 months old. In order to prevent complications from hypothyroidism, the short-term levothyroxine treatment was implemented | Soy-induced hypothyroidism and goiter were totally cured by adequate iodine intake and dietary diversification, validating the clinical suspicion of soy-induced thyroid dysfunction in a toddler with low iodine levels | Caprio et al. (2022) |

Abbreviations: ADHD, attention-deficit hyperactivity disorder; ASD, autism spectrum disorder; CVD, cardiovascular diseases.

(Westmark 2014). Andres et al. (2012) investigated the mental, motor, and linguistic development of infants, whereby 391 healthy participants were breastfed, milk-based formula-fed, or SP-based formula-fed throughout their first year of life. A longitudinal assessment was conducted at 3, 6, 9, and 12 months of age. The Bayley Scales of Infant Development and the Preschool Language Scale-3 were used to assess development. These findings demonstrated that there was no significant difference between the milk-fed and soy-fed groups and that all developmental test results fell within acceptable standard norms. Another result revealed that breastfed newborns had little intellectual growth advantage over formula-fed infants (Andres et al. 2012).

Existing evidence from systematic reviews and regulatory reviews now shows that infant SbF are safe for typical neurodevelopment and cognitive functioning. The FDA, EFSA, and an array of international regulatory authorities all agree that SbF will allow for normal brain development when used as directed (European Union 2024; FDA 2025). A meta-analysis of longitudinal studies found no significant differences in any cognitive outcomes, IQ scores (or similar measures), or neurodevelopmental cognitive milestones between children fed infant SbF compared to those fed Cmilk-based formulas (Bellando et al. 2020). Larger cohort epidemiological studies with long-term follow-up into young adulthood have consistently shown that neurological development across feeding groups is comparable (Ha et al. 2021). Individual studies have identified isolated findings of small differences in some cognitive tests between feeding groups; however, differences fall within the range expected by population norms and lack clinical importance. Moreover, these studies typically had methodological limitations, such as small sample sizes, no adjustment for confounders, or short follow-up periods, all of which should temper interpretability (Kostecka et al. 2021). SbF does contain phytoestrogens, which would be reflected in infant plasma, but the amounts to this effect are much lower than doses required to engage physiological effects based on the dose-response relationships established from toxicological studies (Shapira et al. 2020).

#### 4.1.2 | Immune System

SbF could disrupt the vaccine and immunization process. Compared to controls, infants fed SbF had a poorer immunological response to polio, diphtheria, tetanus, pertussis, and rotavirus vaccinations (Testa et al. 2018). Limiting SP consumption might reduce the generation of immunoglobulins. Infant immunological status is improved when nucleotides are introduced to milk-based formula. Infants fed SbF with and without additional nucleotides for a year were assessed for their immunological state and morbidity by Ostrom et al. (2002). In a 12-month masked feeding process, infants were randomized to groups that received SbF with or without additional nucleotides. Concurrent enrollment included a nonrandomized human milk cohort. At 2, 4, and 6 months, the recommended vaccinations were provided. At 6, 7, and 12 months, antibody responses to the poliovirus, tetanus, diphtheria, and *Haemophilus influenzae* Type B vaccinations were used to evaluate the immune system. The results revealed that infants fed SbF supplemented with and without nucleotides did not exhibit any significant differences in their responses. Nevertheless, compared to infants fed human milk or formula, those fed nucleotide-supplemented soy had greater levels of antibodies against *H. influenzae* Type B at 7 and 12 months. At 12 months, infants fed human milk disclosed greater levels of poliovirus-neutralizing antibodies than infants fed soy milk. As indicated by antibody responses to childhood vaccinations, infants fed SbF demonstrate normal immunological development (Ostrom et al. 2002).

Another study was conducted by the same research team on the populations of immune cells in infants fed SbF with and without additional nucleotides. Infants were also randomized to groups that received SbF with or without additional nucleotides under a 1-year masked feeding trial. Concurrent enrollment included a nonrandomized human milk cohort. Three-color flow cytometry was used to analyze 32 immune cell types. Blood samples were taken at 6, 7, and 12 months. Cellular markers that focus on the development and activation of B, T, and NK cells were selected to evaluate the overall immunological state of infants. The results suggested that the proportion of CD57+ NK T cells at 12 months was the only discernible variation between infants fed SbF and those fed human milk. There was no significant difference in cell populations between infants fed SbF with and without nucleotides. Infants fed SbF indicated immune cell status comparable to infants fed human milk, which is compatible with the normal development of the immune system. Although individual immune cell populations were not significantly influenced by the addition of nucleotides to SbF, it did seem to raise the population of T cells and reduce that of NK cells (Cordle et al. 2002).

The immunity during postnatal development is significantly influenced by intestinal microorganisms. Although the infant's food has an enormous impact on the nature of their gut microbiota, soy-based milk might affect this composition. For instance, the influence of soy-based milk consumption on the infant intestinal ecosystem was determined by Piacentini et al. (2010). Soymilk was used to substitute the formula made from Cmilk for 12 infants. The infant's intestinal microbial composition was examined before and after the change in diet. The findings reveal that SbF feeding does not affect infants' gastrointestinal (GI) microbes or the population of intestinal bifidobacteria (Piacentini et al. 2010).

In a multicenter, randomized, double-blind trial, GI tolerance of two experimental SbF supplemented with fructooligosaccharides was compared to a standard commercial SbF in healthy infants. Healthy-term newborns were recruited for the trial, randomly allocated to one of the three study formulas, and given only the designated study formula from birth to 35 days. The result indicated that study completion rates, growth, stool consistency and frequency, formula intake, vomit, and safety variables were not significantly different. Over the first 35 days of life, infants fed SbF supplemented with short-chain fructooligosaccharides and mixed carotenoids, with or without sucrose, demonstrated good tolerance and hydration equivalent to the control SbF that was considered safe (Lasekan et al. 2015).

Infant SbF do not negatively affect the normal development and function of the immune system, supported by the lack of evidence of any clinically significant immunological deficit.

A number of randomized controlled studies and prospective cohort studies indicated that infants consuming SbF can exhibit normal immune responses and produce antibodies as expected. The strongest evidence came from a systematic review of 15 studies involving >10,000 infants that reported no differences in rates of infection or immune marker profiles and no differences in response to vaccinations in infants fed SbF compared to those fed Cmilk formula. Long-term follow-up studies found similar patterns in terms of immune-related conditions, such as allergies and autoimmune conditions, across the feeding groups (Maryniak et al. 2022). Some studies observing infants consuming SbF reported differences in certain immune parameters, such as cytokine production or concentrations of immunoglobulins. These measurements, though, were all within normal pediatric reference ranges and did not correlate with clinical findings of increased infection susceptibility or altered inflammatory or disease patterns. The clinical relevance of laboratory differences is uncertain, as it is possible that differences observed do not represent functionally relevant changes or clinically meaningful differences in outcomes but that they may reflect normal biologic variation. The current guidelines position pediatricians to continue to recommend SbF as a suitable option for children unable to take Cmilk-based formulas. As this new evidence was discussed by expert panels of health professionals, they reached a consensus that the proposed immune system effects are likely not clinically important (Pomeranz et al. 2018).

#### 4.1.3 | Reproductive System

In humans and rodent models, early exposure to estrogenic chemicals has an impact on the development of the reproductive system. Exposure to soy-containing products, which include phytoestrogens like genistein, can lead to elevated blood concentrations in newborns fed SbF. In an Infant Feeding and Early Development study by Harlid et al. (2017), vaginal cells from soy-fed infant girls were investigated for alteration of DNA methylation in correlation with SbF exposure. Vaginal cells with epigenome-wide DNA methylation were examined from four girls fed with SbF and six girls fed with Cmilk formula. A total of 214 vaginal cell samples were serially obtained from 50 female infants between birth and 9 months of age. Pyrosequencing was used to monitor the two most differentially methylated locations. Infants given SbF and those fed bovine formula had different methylation levels at three CpGs in the gene proline-rich five-like based on the epigenome-wide scan. Pointwise differences between the two feeding groups' methylation levels after 126 days were statistically significant. The modification of DNA methylation in vaginal cells occurred in female infants fed with SbF, and this might have been attributed to a reduction in the expression of an estrogen-responsive gene (Harlid et al. 2017).

In another study, Chin et al. (2021) assessed the relationship between the different dietary patterns of male infants and the hormone-responsive tissues and reproductive hormones. A prospective cohort of mother–infant pairs who fed only SbF, Cmilk formula, or breast milk to their infants throughout research follow-up was included. The hormone-responsive tissues and reproductive hormone samples were collected from 147 baby boys between birth and 28 weeks of age. Mixed-effects regression splines are used to analyze dietary differences in age trends for these results. Infancy exposure to phytoestrogen has no effect on the indicators of early male reproductive development (Chin et al. 2021). Furthermore, prepubescent boys' and girls' sexual development and the beginning of puberty were unaffected by consuming SPS for a year; nevertheless, it could have caused an increase in the girls' height and weight, which would have been linked to changes in fat-free mass (Duitama et al. 2018). The size and anatomical features of the reproductive organs in 5-year-old children, who were part of a long-term cohort study, were investigated by Andres et al. (2015). In 101 children, including 50 boys and 51 girls aged 5 years, the volumes and features of the breast bud, uterus, ovaries, prostate, and testes were evaluated by ultrasonography. These children were breastfed, fed Cmilk formula, or SbF as infants. The finding demonstrated that early infant nutrition did not impact the volumes and anatomical features of the reproductive organs in this cohort of 5-year-olds (Andres et al. 2015).

Longitudinal studies support the conclusion that use of SbF in infancy has no adverse impact on reproductive development and/or function in either males or females. Long-term follow-up studies have evaluated reproductive outcomes since infancy and into adulthood, meaning the conclusions we have drawn from these studies bridge developmental periods. Additional studies have demonstrated similar timing of puberty, hormone levels, and reproductive function across feeding groups (Oliveira et al. 2021; Xiong et al. 2022). Although a few animal studies have suggested the possibility of impact on the basis of very high doses of isolated soy compounds, these studies have not been done with human populations consuming SbF at recommended levels. The extrapolation made based on high-dose animal studies to normal infant dietary consumption is scientifically invalid due to the differences in dosing, metabolism, and timing of development (Suen et al. 2021). Regulatory bodies across the world, including the FDA and Health Canada, have conducted safety assessments and concluded that SbF posed no risk to reproduction when the product is consumed as recommended. These assessments were based on animal safety studies and epidemiological evidence, which include several generations of individuals (Government of Canada 2025).

#### 4.1.4 | Thyroid Gland

Akkaya et al. (2020) determined the impact of different amounts of infant SbF on the histological and physiological functions of the thyroid gland. Four groups of 28 female Sprague-Dawley rats were prepared. Rats were fed with regular pellet feed, infant SbF, low-dose SbF, and high-dose SbF. Blood samples were collected on days 0, 30, 60, and 90. Rats fed high-dose SbF exhibited significantly higher serum levels of free triiodothyronine, free thyroxine, thyroid-stimulating hormone, antithyroglobulin antibody, and anti-troponin antibody than the other groups. Histopathological results between the four groups did not differ from one another. High infant SbF caused hyperthyroidism and elevated thyroid-stimulating hormone levels. Elevated levels of antithyroglobulin antibody and anti-troponin antibody indicate that the observed alterations may have been caused by inflammation (Akkaya et al. 2020).

Concerns have been raised that SbF consumption may negatively impact thyroid function in people who are iodine-deficient or have subclinical hypothyroidism. The first Italian case of soy-induced goiter and hypothyroidism has been reported by Caprio et al. (2022). A boy toddler at the age of 22 months, who had previously been diagnosed with a Cmilk allergy, appeared at the clinic with significant goiter and overt hypothyroidism. Following a thorough nutritional evaluation, it was discovered that he had been following a strict soy milk-based diet since he was 12 months old. To prevent complications from hypothyroidism, the short-term levothyroxine treatment was implemented. Soy-induced hypothyroidism and goiter were totally cured by adequate iodine intake and dietary diversification, validating the clinical suspicion of soy-induced thyroid dysfunction in a toddler with low iodine levels. To prevent nutritional deficiencies in children on a limited diet because of various food allergies, this case emphasized the significance of thoroughly examining dietary habits and providing adequate micronutrient supplements (Caprio et al. 2022).

Clinical data show that infant SbF do not produce clinically significant thyroid dysfunction when adequate iodine levels are maintained. When infant SbF include a source of iodine and is designed to iodine levels that support normal thyroid function, there are no clinical impacts on thyroid function (Singh et al. 2024). Multiple prospective studies have shown normal serum thyroid hormone levels and normal thyroid function tests in infants and children consuming SbF with an adequate iodine source (Segni 2017). Furthermore, a systematic review of infants consuming SbF found no evidence of increased thyroid disorders or abnormal serum thyroid hormone levels compared with controls (Wiesner et al. 2021). For decades, concerns about the impacts of soy and thyroid function have arisen primarily based on settings of iodine deficiency and cases of iodine deficiency that occurred when SbF were not iodine-fortified. Modern SbF include adequate iodine in precise amounts that meet or exceed recommendations for dietary allowances in infants (Messina, Duncan, et al. 2022). Various in vitro studies have suggested that soy products may alter thyroid hormone production under certain laboratory conditions. However, lab conditions do not reflect the physiological conditions of formula-fed infants, and there are no clinical studies demonstrating meaningful effects on thyroid function when adequate iodine is provided (Testa et al. 2018). Current pediatric endocrinology guidelines recommend routine thyroid monitoring for all infants regardless of their feeding method, and there are no recommendations for SbF-fed infants other than ensuring their adequate iodine intake.

#### 4.1.5 | Safety Assessment

The safety of infant SbF was examined in children for anthropometric development, immunity, bone health, cognition, reproductive, and endocrine functioning by Lee et al. (2024). The evaluation included cross-sectional, case-control, cohort, or clinical studies. Children who were fed infant SbF showed anthropometric patterns that were comparable to those of children who were fed Cmilk-based formulas or human milk. Although infant SbF had significant amounts of phytates, the bone mineral content, serum protein, zinc, calcium concentrations, and hemoglobin were comparable to children given the other two types of milk (Lee et al. 2024). Children given infant SbF also had higher levels of genistein and daidzein, but there is no compelling evidence of a detrimental impact on endocrine and reproductive functions. Neurocognitive measures and immunological indicators were comparable across all feeding groups. The findings showed that current infant SbF are safe, evidence-based choices for feeding infants and children with nutritional requirements. Children fed with these three types of milk have equivalent growth, bone health, metabolic, reproductive, endocrine, immunological, and neurological characteristics (Vandenplas et al. 2014).

### 4.2 | In Adults

Adults who consume SP often experience many nutritional benefits because it is a complete protein supply that contains every necessary AA, is free of cholesterol, is and low in saturated fat (Table 4). Besides, SP is rich in B vitamins, calcium, zinc, iron, and unique isoflavones classified as phytoestrogens and has been reported to improve health. SP could reduce levels of LDL-C, lower blood pressure, decrease cancer risk, and enhance bone health, especially in postmenopausal women. Nonetheless, current research has mostly addressed previously raised concerns regarding soy's impact on hormones. There have been claims that soy feminizes men since it includes isoflavones. Clinical data were examined by Reed et al. (2021) to investigate the impact of soy and isoflavones on hormone levels. The meta-analysis included 141 articles and 38 clinical trials that were judged appropriate for inclusion. The result indicated that there were no significant effects of soy or isoflavones on male testosterone or estrogen levels (Reed et al. 2021). There is no solid proof that moderate soy intake impairs thyroid function in healthy individuals. The majority of healthy adults seem to tolerate 25–50 g SP/day. Although individual reactions may differ according to gut microbiota and genetics, those with certain soy sensitivities should avoid it. People with certain thyroid disorders might wish to consult with medical professionals (Messina, Duncan, et al. 2022).

#### 4.2.1 | Cardiovascular Diseases

The main reason for mortality is CVDs, which might be caused by high blood pressure, obesity, diabetes, increased low-density lipoprotein cholesterol (LDL-C), reduced HDL-C, elevated cholesterol, and hypertriglyceridemia. Many studies have examined the relationship between SP consumption and cardiovascular health, which has yielded significant findings regarding cholesterol reduction and heart disease risk in adults. Intact dietary strategies to lower triglyceride and LDL-C levels and alleviate the effects of CVD were determined. Age at death, all-cause mortality, and saturated fat intake are all correlated with cholesterol levels on the basis of the findings among seven countries under a 50-year monitoring program (Demirci et al. 2020; Liorančas and Lee 2024). Although LDL-C levels rose, saturated lipids did not raise CVD risk (CVR), whereas refined carbohydrates did. Healthy complex carbohydrates from plant-based diets decreased CVD. The result displayed that omega-3 fatty acids (OFAs) decreased triglycerides by 21.6% and CVD by 26.1%. Coronary plaque development was inhibited by an OFA index of at least 4%, which included docosahexaenoic

TABLE 4 | Health benefits of soy-based formula (SbF) in adults.

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | References |
|---|---|---|---|---|---|
| **Cardiovascular disease** | | | | | |
| Heart diseases | The influence of soy isoflavones on CVD indicators is determined in postmenopausal women | 200 women with an average age of 55 years | A double-blind, randomized, parallel study was used to estimate the predicted 10-year risk of CVD and mortality. The women were randomly assigned to receive an SP or isoflavone-containing snack bar between meals every day for 6 months | The estimated reductions in these risks with isoflavone treatment at 6 months were 27% in coronary heart disease in 10 years, 37% in myocardial infarction, 24% in CVD, and 42% in CVD death. Supplementing with SP containing isoflavones for 6 months resulted in a substantial improvement in CVD indicators and estimated CVD at 6 months during the early stages of women's menopause | Sathyapalan et al. (2018) |
| Cardiovascular disease | A population-based cohort research was conducted in Japan to investigate the association between CVD mortality and consumption of natto, SP, and soy isoflavones | 15,724 female and 13,355 male Takayama Study participants at least 35 years old | A validated semiquantitative food-frequency questionnaire was given to each participant. Across 16 years, deaths from CVD were determined. | A lower risk of mortality from all CVD was substantially linked to the highest natto consumption in contrast to the lowest consumption. A reduced likelihood of mortality from a total stroke was significantly linked to the highest consumption of natto and total SP | Nagata et al. (2017) |
| Coronary artery disease | The correlation between soy product consumption and CVD was also determined in Chinese individuals | A total of 512,891 adults aged 30–79 were enrolled. 22,923 participants with a history of CVD and 487,034 participants without CVD were included | Utilizing a food frequency questionnaire, information on soy product consumption has been obtained. The cardiovascular mortality hazard ratios linked to soy product consumption were estimated using Cox regression | Those without a history of cardiovascular disease who consumed soy at least 4 days a week had a significantly decreased risk of suffering from an acute myocardial infarction compared to those who consumed it infrequently or never; an increased consumption of soy products was not related to cardiovascular mortality in those with a history of CVD | Wang et al. (2021) |
| **Menopausal symptoms** | | | | | |
| Menopausal symptoms | The influence of the SP diet on the menopausal symptoms of women was evaluated in a few rural Karur communities in India | 60 menopausal women | Sixty grams of soybeans were administered to 60 menopausal women every day for 4 weeks | Menopausal women who consume 60 g SP/day would have relatively mild menopausal symptoms | A. Thankachan (2020) |

(Continues)

**TABLE 4** | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | References |
|---|---|---|---|---|---|
| **Cardiovascular disease** | | | | | |
| Perimenopausal symptoms | The influence of SP on women's perimenopause symptoms was investigated | 40 women with perimenopausal symptoms were divided into the experimental and control groups | Participants in the trial received 150 mL of milk containing 1 g of soy powder every morning and evening for 15 days | Women's perimenopause symptoms were demonstrated to be effectively reduced by soy powder. This suggests that in order to retain the women's normal status, alternative therapy must be considered | T. T. Jose and Raghavan (2020) |
| Facial signs of photoaging and skin hydration | The effects of soy protein isolate (SPI) with isoflavone supplementation were examined on skin biophysical variables and as photoaging characteristics in postmenopausal women | 44 postmenopausal women with Fitzpatrick skin Types I, II, and III | 44 women received either isoflavones or casein protein orally in this 6-month prospective, randomized, double-blind. The degree of wrinkles and pigmentation was measured at 0, 8, 16, and 24 weeks using high-resolution facial photography. Sebum production and skin moisture measured biophysically | Supplementing with dietary SP that contains isoflavones could assist these postmenopausal women with photoaging, such as wrinkles and dyspigmentation, and enhance skin moisture | Rizzo et al. (2023) |
| Menopausal symptoms | The association was evaluated between the age at which menopause naturally occurs, the symptoms it causes, and diets rich in protein and different nutritional supplements | 52,347 individuals between the ages of 35 and 60, with a median age of 50 years old and an average age of 49.46 | Participants have been selected from 13 cities in 12 provinces in China using a multistage stratified random sampling technique in the large-scale cross-sectional survey | Soy products may have a beneficial effect on symptomatic relief, especially in terms of alleviating physical and psychological symptoms to alleviate menopausal symptoms, and offer beneficial alternatives for perimenopausal women's dietary interventions | Yang et al. (2025) |
| **Cancer prevention** | | | | | |
| Prostate cancer | There was a secondary investigation of clinical chemistry, thyroid hormones, blood pressure, body weight, and iron status in a 2-year trial of SP supplementation | 93 eligible men between the ages of 44 and 75 in New York, US. They were at risk of cancer recurrence after prostatectomy | Subjects were randomized to either soy or a casein-based placebo for dietary supplementation with 20 g/day SPI containing 41 mg total isoflavones and 23 mg genistein. Blood samples, blood pressure, and weight were taken every 2 months in year 1 and every 3 months in year 2 | Serum total cholesterol, calcium, phosphorus, iron status indicators, thyroid hormones, body weight, and blood pressure were unaffected by consuming 2-year SP supplements compared to a casein-based placebo | Bosland et al. (2021) |

(Continues)

TABLE 4 | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | References |
|---|---|---|---|---|---|
| **Cardiovascular disease** | | | | | |
| Prostate cancer | The impact of soy was determined on the risk of recurrence of prostate cancer after radical prostatectomy in middle-aged and elderly patients | 159 eligible Caucasian males between the ages of 47 and 74 in New York, US | The 2-year randomized trial using SPI was conducted in comparison to a milk protein placebo for examination of growth hormone/insulin-like growth factor-1 axis biomarkers, apoptosis and angiogenesis, testosterone, sex hormone-binding globulin, and estradiol | Middle-aged to older men who consumed 19.2 g/day of whole SPI with 24 mg of genistein for 18 months demonstrated a decrease in circulating testosterone and sex hormone-binding globulin, but not free testosterone, as compared to the casein-based placebo | Bosland et al. (2022) |
| Breast cancer | The risk of breast cancer is investigated in relation to soy and dairy consumption | 52,795 women with a mean age of 57.1 from North America who were originally cancer-free and monitored for 7.9 years make up the study group, with 29.7% of Black women | 6 structured 24-h meal recalls and food frequency questionnaires were used to estimate dietary intakes for 1011 calibration research participants | After controlling for soy consumption, higher dairy milk intakes were found to contribute to an increased risk of breast cancer | Fraser et al. (2020) |
| Breast cancer | The association between soy intake levels and breast cancer cases was explored | Over 300,000 female participants aged 30–79 from 10 regions across China for 10 years of follow-up | The examination of data from the China Kadoorie Biobank project and the integration of existing evidence through a dose-response meta-analysis in the large cohort study were used | A 3% lower incidence of breast cancer was associated with each 10 mg/day of soy isoflavone consumption. Higher soy consumption may offer potential improvements in preventing breast cancer instead of low or moderate soy intake | Wei et al. (2020) |
| Cervical cancer | The direct and possible interactive effects of soy and tea consumption on the risk of cervical cancer were examined | 30,744 Singaporean Chinese women with a median follow-up interval of 16.7 years and 312 incident cervical cancer cases | A subanalysis for a nested case-control study in a prospective population-based cohort with evaluation of human papillomavirus serological status | The ability of soy to prevent the development of cervical cancer may rely on the components of green tea | Paul et al. (2019) |
| **Osteoporosis** | | | | | |
| Osteoporotic metabolism | The influence of SP on lipid profiles and inflammatory and osteoporotic metabolism was assessed | 135 mobile individuals, 65 men and 70 with ages between 27 and 87 | Participants had 40 g daily consumption of casein or SP for 3 months. A fasting venous blood sample of 20 mL, height, weight, and percent body fat were collected | SP supplements used regularly may improve body composition and bone metabolism | George et al. (2020) |

(Continues)

**TABLE 4** | (Continued)

| Health concern | Clinical trial | Human participants | Study design | Significant outcome | References |
|---|---|---|---|---|---|
| **Cardiovascular disease** | | | | | |
| Osteoporotic fracture | The interactions between the risk of osteoporotic fractures and dietary intakes of soy isoflavones were investigated | 61,025 Shanghai men aged 40–74 years participated for a median follow-up of 9.5 years | In-person questionnaires were used to monitor the cohort for major illnesses, the incidence of bone fractures, and survival status. The incidence of osteoporotic and non-osteoporotic fractures was multivariable and examined using Cox regression | A high intake of soy isoflavones was linked to a lower incidence of osteoporotic fractures in males, regardless of recognized protective or risk variables, including dietary consumption of calcium and magnesium | Cui et al. (2022) |
| Osteoporosis | Plasma bone turnover and cardiovascular risk markers were accessed | 200 women within 2 years of the start of menopause | Participants were randomly assigned to receive 15 g SP with 66 mg of isoflavone or 15 g SP only daily for 6 months in the double-blind, randomized parallel trial | There was a significant reduction of the resorption and formation in bone turnover markers and an improvement in cardiovascular risk indicators. It suggested that consuming soy with isoflavones may positively impact bone health by first decreasing osteoclast function and then decreasing osteoblast function | Sathyapalan et al. (2017) |

Abbreviations: ADHD, attention-deficit hyperactivity disorder; ASD, autism spectrum disorder; CVD, cardiovascular diseases.

and eicosapentaenoic acids. Consumers should keep consuming fewer refined carbohydrates and saturated fats, eliminate trans fats, and eat more fruits, vegetables, whole grains, low-fat dairy, fish, and other OFAs. CVD can be reduced significantly by following a Mediterranean diet (Lee et al. 2016; Welty 2020).

For postmenopausal women, hormone replacement treatment may help lower their risk of CVR. The influence of soy isoflavones on CVD indicators is determined. In a recent study by Sathyapalan et al. (2018), a double-blind, randomized, parallel study with 200 women with an average age of 55 years in the early stages of menopause was used to estimate the predicted 10-year risk of CVD and mortality. The women were randomly assigned to receive an SP or an isoflavone-containing snack bar between meals every day for 6 months. The Framingham CVR engine was utilized to determine CVR on the basis of factors such as age, blood pressure, lipid profiles, diabetes, and smoking. The estimated reductions in these risks with isoflavone treatment at 6 months were 27% in coronary heart disease in 10 years, 37% in myocardial infarction, 24% in CVD, and 42% in CVD death. When compared to SP without isoflavones, supplementing with SP containing isoflavones for 6 months resulted in a substantial improvement in CVR indicators and estimated CVR at 6 months during the early stages of women's menopause (Sathyapalan et al. 2018).

A substantial fibrinolytic enzyme is found in natto, a traditional Japanese soy product. A population-based cohort research was conducted in Japan to investigate the association between CVD mortality and consumption of natto, SP, and soy isoflavones (Nagata et al. 2017). There were 15,724 female and 13,355 male Takayama Study participants, who were at least 35 years old. A validated semiquantitative food-frequency questionnaire was given to each participant. Across 16 years, deaths from CVD were determined. A lower risk of mortality from all CVD was substantially linked to the highest natto consumption, in contrast to the lowest consumption. A reduced likelihood of mortality from a total stroke was significantly linked to the highest consumption of natto and total SP (Sathyapalan et al. 2018). Wang et al. (2021) also determined the correlation between soy product consumption and CVD in Chinese individuals. A total of 22,923 participants with a history of CVD and 487,034 participants without CVD were included. Utilizing a food frequency questionnaire, information on soy product consumption has been obtained. The cardiovascular mortality hazard ratios linked to soy product consumption were estimated using Cox regression. Those without a history of CVD who consumed soy at least 4 days a week had a significantly decreased risk of suffering from an acute myocardial infarction compared to those who consumed it infrequently or never. An increased consumption of soy products was not related to cardiovascular mortality in those with a history of CVD (Wang et al. 2021).

#### 4.2.2 | Menopausal Symptoms

The majority of women experience mild perimenopausal symptoms, including hot flashes, heart pain, insomnia, depression, agitation, anxiety, physical and mental fatigue, vaginal dryness, sexual dysfunction, bladder problems, and joint and muscle pain. Many studies on the effects of SP on menopausal symptoms presented that whole soy foods are preferred over isolated supplements, and consistent daily consumption appears more effective than intermittent intake. Besides, benefits may continue with long-term use, and the best results could be observed when the SP is part of an overall healthy diet pattern. Multiple clinical trials show a moderate reduction in hot flash frequency (20%–45%) with daily SP intake. The most effective dosage appears to be 20–60 g of SP containing 40–80 mg isoflavones. A response is typically observed after 4–12 weeks of consistent consumption (Qin et al. 2022).

The influence of SP on women's perimenopause symptoms was investigated in a recent study by T. T. Jose and Raghavan (2020). A total of 40 women with perimenopausal symptoms were divided into the experimental and control groups, with 20 women in each group. Participants in the trial received 150 mL of milk containing 1 g of soy powder every morning and evening for 15 days. Women's perimenopause symptoms were shown to be effectively reduced by soy powder. This suggests that, to retain the women's normal status, alternative therapy must be considered (T. T. Jose and Raghavan 2020). The three most significant inflammatory markers are interleukin-6, C-reactive protein, and tumor necrosis factor-alpha (TNF-$\alpha$). However, the impact of SP and isoflavones on postmenopausal women's blood levels of TNF-$\alpha$ and interleukin-6 was not significantly supported by another meta-analysis (Gholami et al. 2022).

One specific phase of the female reproductive life cycle is menopause. The influence of the SP diet on the menopausal symptoms of women was evaluated in a few rural Karur communities in India (T. Aby 2020). Sixty grams of soybeans were administered to 60 women every day for 4 weeks. The same Heinemann Menopausal Rating Scale was used for the pretest and posttest on the first day of the intervention and the first day of the fifth week, respectively, for both groups. Findings indicated that the effectiveness of SP consumption was responsible for the posttest mean level of menopausal symptoms. Menopausal women who consume 60 g SP/day might experience menopausal symptoms that are mild and significantly less severe than those of other women (T. Aby 2020).

Rizzo et al. (2023) examined the effects of SPI with isoflavones supplementation on skin biophysical variables and photoaging characteristics in postmenopausal women. There were 44 postmenopausal women with Fitzpatrick skin Types I, II, and III, who were assigned to receive either isoflavones or casein protein in this 6-month prospective, randomized, double-blind study. The degree of wrinkles and pigmentation was measured at 0, 8, 16, and 24 weeks using high-resolution facial photography equipment. Sebum production and skin moisture were measured biophysically. The results revealed that supplementing with dietary SP containing isoflavones could assist these postmenopausal women with photoaging, such as wrinkles and dyspigmentation, and enhance skin moisture (Rizzo et al. 2023). The association between the age at which menopause naturally occurs, the symptoms it causes, and diets rich in protein and different nutritional supplements was evaluated in another study (Yang et al. 2025). A total of 52,347 individuals between the ages of 35 and 60 were selected from 13 cities in 12 provinces in China using a multistage stratified random sampling technique in the large-scale cross-sectional survey. The female population's median age at natural menopause was 50 years, and the average age was 49.46 years. The results demonstrated a strong negative correlation between the severity of menopausal symptoms and the consumption of soy products. This suggests that soy products may have a beneficial effect on symptomatic relief, especially in terms of alleviating physical and psychological symptoms, alleviating menopausal symptoms, and offering beneficial alternatives for perimenopausal women's dietary interventions (Yang et al. 2025).

There have been a number of clinical trials using different isoflavone sources, such as red clover and soy, and almost all of the studies with suitable designs have shown results supporting isoflavone supplementation. There are no speculated negative consequences from a possible interaction of isoflavones with hormone-sensitive tissues in the thyroid, uterus, or mammary gland based on the human trial that is currently available. Long-term consumption of up to 150 mg of isoflavones/day for at least 3 years was safe. Furthermore, it has been shown that consuming a lot of isoflavones could mitigate the risk of breast cancer. Clinical results suggest that exposure to isoflavones may have advantages even when tamoxifen is being used to treat breast cancer (Schmidt et al. 2016).

#### 4.2.3 | Cancer

The American Cancer Society's current cancer prevention guidelines state that the consumption of soy foods is safe for cancer survivors and may even be protective (American Cancer Society 2025). However, because the guidelines are based on past concerns about phytoestrogens, they are tentative and therefore conservative. On the basis of our broader review of recent research, the guidelines may still be overly conservative and in need of professional guidance updates as new evidence is being published. There is also a wider variation of recommendations for soy in the international guidelines for cancer prevention. For example, the Japanese cancer prevention guidelines expressly encourage soy consumption as part of a traditional dietary pattern. European guidelines have more neutral recommendations. The research evidence will broaden in terms of diet, population, and timing of exposure; also genetic factors influencing isoflavone metabolism should also be considered in future guideline development (Nakai et al. 2020).

Associations between soy or dairy intake and breast cancer risk are inconsistent. The combined findings demonstrated that, when comparing extreme categories of soy intake, a higher soy intake was substantially linked to a 10% lower risk of total cancer incidence (Fan et al. 2022). The risk of breast cancer was investigated by Fraser et al. (2020) in relation to soy and dairy consumption. 52,795 women with a mean age of 57.1 from North America who were originally cancer-free and monitored for 7.9 years make up the study group, with 29.7% of Black women. Six structured 24-h meal recalls and food frequency questionnaires were used to estimate dietary intakes for 1011 participants under calibration research. After controlling for soy consumption, higher dairy milk intakes were found to contribute to an increased risk of breast cancer (Fraser et al. 2020). Through the examination of data from the China Kadoorie Biobank project and the integration of existing evidence through a dose-response meta-analysis in a large cohort study, the association between soy intake levels and breast cancer cases was explored in over 300,000 female participants aged 30–79 from 10 regions across China for 10 years of follow-up (Wei et al. 2020). A 3% lower incidence of breast cancer had been associated with each 10 mg/day of soy isoflavone consumption. Increased soy consumption may offer potential improvements in preventing breast cancer instead of low or moderate soy intake (Wei et al. 2020). The direct and possible interactive effects of soy and tea consumption on the risk of cervical cancer were examined in 30,744 Singaporean Chinese women with a median follow-up interval of 16.7 years and 312 incident cervical cancer cases. The results implied that the ability of soy to prevent the development of cervical cancer may rely on the components of green tea (Paul et al. 2019).

To evaluate the impact of soy on the risk of recurrence of prostate cancer after radical prostatectomy in middle-aged and elderly patients, there was a secondary investigation of clinical chemistry, thyroid hormones, blood pressure, body weight, and iron status in a 2-year randomized controlled trial of SP supplementation (Bosland et al. 2021). Men aged 44–75 who were at risk of cancer recurrence after prostatectomy were randomized to either soy or a casein-based placebo for dietary supplementation with 20 g/day SPI, which provided 41 mg/day total isoflavones and 23 mg/day genistein. Blood samples, blood pressure, and weight were taken every 2 months in the first year and every 3 months in the second year. Serum total cholesterol, calcium, phosphorus, iron status indicators, thyroid hormones, body weight, and blood pressure were all unaffected through consuming 2-year SP supplements compared to a casein-based placebo (Bosland et al. 2021). The same research team continued their study on the 2-year randomized trial using SPI in comparison to a milk protein placebo. The impact of SP was assessed on growth hormone/insulin-like growth factor-1 axis biomarkers, apoptosis, and angiogenesis, as well as on the steroid hormones—testosterone, sex hormone-binding globulin, and estradiol—that are implicated in prostate cancer. Participants were 159 eligible Caucasian males between the ages of 47 and 74 in New York, USA. The finding exhibited that middle-aged to older men, who consumed 19.2 g/day of whole SPI with 24 mg genistein for 18 months, demonstrated a decrease in circulating testosterone and sex hormone-binding globulin but not free testosterone, as compared to the casein-based placebo (Bosland et al. 2022).

#### 4.2.4 | Osteoporosis

Studies have demonstrated that SP lowers cholesterol, and its isoflavones could assist with maintaining healthy bones. The influence of SP on lipid profiles, inflammation, and bone metabolism was estimated in 90 women and men at ages between 27 and 87 with 40 g daily consumption of casein or SP for 3 months. The results displayed that SP consumption significantly increased serum insulin-like growth factor-I and decreased bone alkaline phosphatase, body fat percentage, and tartrate-resistant acid phosphatase. This indicates that regular SP supplements may improve body composition and bone metabolism (George et al. 2020). Moreover, the interactions between the risk of osteoporotic fractures and dietary intakes of soy isoflavones were investigated by Cui et al. (2022) in Shanghai in 61,025 men aged 40–74 years for a median follow-up of 9.5 years. In-person questionnaires were used to monitor the cohort for major illnesses, the incidence of bone fractures, and survival status. The hazard ratio and 95% confidence interval were used to assess the relationships between the variables under investigation for dietary consumption of soy isoflavones and the incidence of osteoporotic and non-osteoporotic fractures using multivariable Cox regression. The results presented that a high intake of soy isoflavones was linked to a lower incidence of osteoporotic fractures in males, regardless of recognized protective or risk variables, including dietary consumption of calcium and magnesium (Cui et al. 2022). A study also investigated plasma bone turnover and cardiovascular risk markers in 200 women within 2 years of the start of menopause (Sathyapalan et al. 2017). Participants were randomly assigned to receive 15 g SP with 66 mg isoflavone or 15 g SP only every day for 6 months in the double-blind, randomized parallel trial under the assessment of insulin resistance, blood pressure, and lipid profile. The results revealed a significant reduction in the resorption and formation of bone turnover markers as well as an improvement in cardiovascular risk indicators. It suggested that consuming soy with isoflavones may have a positive impact on bone health by first decreasing osteoclast function and then decreasing osteoblast function (Sathyapalan et al. 2017).

## 5 | Nutritional and Functional Properties of SPs

### 5.1 | Digestibility Compared to Other Protein Sources

The nutritional functionality of SP highly promotes its use in health-focused food and beverage formulations. Due to their EAA content and functional properties, SPs can contribute to the nutritional and sensorial quality of plant-based products. Technofunctional properties, including high solubility in neutral and alkaline pH, water-holding capacity, emulsification, and gelation capabilities, make SPs favorable for food and beverage formulations. Protein content and quality and nutritional value of SPs can be modified through various treatments to serve different SbF, revealing varied patterns of protein hydrolysis and digestibility.

$P_{Digest}$ is assessed through ingestible AA composition, the hydrolysis degree of protein in the body, and the availability of AAs for utilization in the body after digestion and absorption (Qin et al. 2022). DIAAS is known as the common descriptor of $P_{Digest}$. Higher $P_{Digest}$ rates are well correlated with better health benefits. Due to their advantages in providing EAAs and advanced GI digestibility, AnPr have been generally regarded as possessing better nutritional value than PDPs, thus playing a crucial role in the human diet. However, recent trends encourage the utilization of PDPs as perceived healthier and supporting sustainable production (Kaur et al. 2022). Soybean is a well-accepted meat alternative due to its excellent protein quality and digestibility. Besides, various physical, chemical, enzymatic, and microbial treatments can induce the generation of the desirable nutritional content and functionality of soy and other PDPs. $P_{Digest}$ is strongly associated with the protein molecular structure, especially secondary structure elements such as $\alpha$-helices and $\beta$-sheets, and turns (Vanga et al. 2020). Conformational changes in these structures due to various treatments can modify the digestibility of SP. It is most probably related to the exposure or masking of EAAs. For instance, prolonged heating was found to cause protein aggregation and limit SP accessibility to cleavage sites (Rivera del Rio et al. 2022). A high proportion of the 7S fraction exhibited diminished digestibility of SbF due to the presence of amyloid aggregate structures (Yang et al. 2016).

The rate of $P_{Digest}$ can be rapid, slow, and resistant based on the protein source and molecular structure. In comparison to PDPs, AnPr generally have higher DIAAS, with some exceptions like SP possessing slightly lower DIAAS. SP has a faster digestion rate than casein but slower than whey proteins. SPI showed a higher rate of postprandial AA level in the blood than the insect proteins (Vangsoe et al. 2018). Formulations are also effective on digestion patterns. For instance, SPI has higher digestibility than SP (Schimbator et al. 2020). Although having the same total protein content, $P_{Digest}$ in a ground beef product (85%) is higher than a soy-based alternative product (70%), possibly due to process and food matrix effects (Zhou et al. 2021). Hydrolysis and digestibility of SP are influenced by the food matrix effect as well as the size and surface area of the protein particles, revealed through treatments in different SbF and soy flours (Reynaud et al. 2020; Zahir et al. 2018). The protein quality of soy milk due to digestibility rate and DIAAS value was found to be comparable with Cmilk and some other plant-based alternatives (Martínez-Padilla et al. 2020; Reynaud et al. 2021).

Another reason for the lower digestibility of PDPs than AnPr is the presence of ANFs in PDPs. Soybean meal has some ANFs like phytates, tannins, and trypsin inhibitors, limiting and/or destroying nutrient digestion and absorption. Trypsin inhibitors lower the biological activity of digestion enzymes like trypsin and chymotrypsin, thus reducing $P_{Digest}$ (Kuenz et al. 2022). Glycinin, $\beta$-conglycinin, and lectin are other macromolecular proteins of ANFs in soybean meals. Glycinin and $\beta$-conglycinin can induce an allergenic response affecting the intestines. Lectins can lead to irritation in the intestines as well. Resultantly, reduced nutrient absorption, intestinal inflammation, and impaired digestion patterns are noticed (Cao et al. 2024). Processing methods like germination, cooking, microwaving, spray drying, freezing, ultrasound, irradiation, and fermentation are promising to downgrade and eliminate the presence of these factors, which then enhance protein quality, facilitate higher levels of digestibility, and bioaccessibility of nutrients (Sá et al. 2020). Soluble oligosaccharides and dietary fibers in soybeans can promote the growth of *Bifidobacterium* in the intestines, thus supporting nutrient digestion and absorption (Pan et al. 2018).

### 5.2 | Bioavailability

#### 5.2.1 | Absorption Studies

SP is available in various forms, primarily as SPI and SPC. These forms differ in their protein content and the presence of other components, which influence nutrient absorption. SPI is highly refined, containing approximately 90% protein, with most fats and carbohydrates removed during processing (Joseph et al. 2018). In contrast, SPC contains about 70% protein, with some carbohydrates and fats remaining (Joseph et al. 2018).

These compositional differences impact nutrient bioavailability. Research indicates that SPI generally has a higher AA absorption rate than SPC due to its higher protein content and reduced nonprotein components (Rutherfurd et al. 2015). A study by Rutherfurd et al. (2015) demonstrated that SPI has a higher digestibility score compared to SPC, meaning AAs are more efficiently absorbed and utilized. This is particularly beneficial for individuals with higher protein needs, such as athletes or those recovering from illness. The superior digestibility of SPI is largely attributed to its lower fiber content, allowing for more efficient breakdown and absorption of AAs in the GI tract (Zheng et al. 2022).

Recent studies further support these findings. Krishnan et al. (2022) reported that SPI has a higher PDCAAS and DIAAS compared to SPC (Ahsan et al. 2018). These scores highlight SPI's superior nutritional value, particularly for muscle protein synthesis and overall health. However, SPC has its own advantages. Its fiber content, although slowing digestion, can provide a sustained release of AAs and other nutrients, which helps regulate blood sugar levels and promote satiety (Loveday 2023). Additionally, dietary fiber, in SPC, supports gut microbiota composition, fostering beneficial bacteria that aid digestion and nutrient absorption (Zheng et al. 2022).

Comparative studies highlight these absorption differences. For example, Aguilera (2019) found that the rapid AA absorption from SPI makes it ideal for post-exercise recovery, quickly replenishing AA levels in the bloodstream. Conversely, SPC's slower digestion provides prolonged nutrient release, beneficial for sustained energy levels. The choice between SPI and SPC depends on individual dietary needs and health goals. For those requiring rapid protein absorption, such as athletes, SPI is the preferred option. Meanwhile, SPC may be more suitable for individuals focusing on gut health and maintaining steady energy levels due to its fiber content and slower digestion rate.

### 5.2.2 | Impact of Food Matrix

**5.2.2.1 | Interactions With Other Foods.** The presence of other foods can significantly impact soy nutrient absorption. The food matrix consumed alongside SP exerts a critical influence on nutrient bioavailability, with effects that can be either antagonistic or synergistic. A primary consideration is dietary fiber, commonly present in whole foods like fruits, vegetables, and whole grains. On one hand, soluble and insoluble fibers can sequester minerals such as calcium, zinc, and iron through adsorption or chelation, forming insoluble complexes and thereby reducing their bioavailability (Güzeler and Yıldırım 2016). Viscous fibers may also slow gastric emptying and decrease the diffusion of nutrients toward the intestinal epithelium, further influencing absorption dynamics. On the other hand, fiber fermentation by the gut microbiota produces short-chain fatty acids (SCFAs), which can enhance colonic mineral absorption and support the release of bioactive metabolites from SP and soy peptides (Thrane et al. 2017). The fermentable fraction of dietary fiber, such as inulin and fructooligosaccharides, can have a positive indirect effect. This fiber serves as a prebiotic, stimulating the growth of beneficial gut microbiota such as *Bifidobacterium* and *Lactobacillus*, which produce SCFAs like butyrate, lowering luminal pH. This acidic environment can improve the solubility and absorption of certain minerals, potentially counteracting the inhibitory effects of phytate (Scholz-Ahrens et al. 2007).

Beyond fiber, the macronutrient composition of a meal also modulates SP nutrient absorption. The co-ingestion of lipids enhances the bioavailability of fat-soluble isoflavones and vitamins from SP (e.g., vitamin D if fortified). Furthermore, the presence of vitamin C-rich foods, such as citrus fruits and bell peppers, can reduce ferric iron ($Fe^{3+}$) to the more absorbable ferrous form ($Fe^{2+}$), thereby mitigating the inhibitory effect of phytate on iron absorption (Teucher et al. 2004). Therefore, the overall impact of a mixed meal on SP nutrient absorption is a complex interplay between inhibitory compounds and enhancing agents, with the net effect dependent on the specific food combinations.

**5.2.2.2 | Enhancement and Inhibition of Nutrient Absorption.** Dietary fiber can act as a physical barrier, slowing digestion and nutrient absorption (Zhang et al. 2022). This delayed digestion helps maintain steady blood sugar levels and prolongs satiety. However, Güzeler and Yıldırım (2016) noted that fiber can also bind minerals like calcium and iron, forming insoluble complexes that hinder absorption. This dual role highlights the need to consider overall dietary composition when evaluating nutrient bioavailability. SP's interaction with other foods can also affect gut microbiota. Fiber-rich foods encourage the growth of beneficial bacteria, which, in turn, improve nutrient absorption (Singh and Kim 2021). Zheng et al. (2022) found that the fiber in SPC enhances gut microbiota composition, promoting beneficial bacteria that support digestion and overall gut health.

**5.2.2.3 | Matrix Effects on Nutrient Release.** The food matrix significantly affects nutrient release and absorption during digestion. For example, the presence of fats in a meal enhances the absorption of fat-soluble vitamins and isoflavones from soy (Iddir et al. 2022). Fats increase the solubility of these nutrients, making them more readily available for absorption. This underscores the importance of considering meal composition when evaluating soy nutrient bioavailability. Figure 1 illustrates the role of the food matrix in nutrient bioavailability. Aguilera (2019) explores scale sensitivity and compound specificity through food examples. In bread, the porous structure influences nutrient release, whereas in milk, the interaction of proteins, fats, and carbohydrates affects nutrient availability. These examples highlight how food microstructure is crucial to digestion and absorption.

The complexity of the food matrix can also influence digestion speed. Foods with intricate structures may slow digestion, leading to a gradual release of nutrients, which can help maintain nutrient levels over time. This controlled release can be particularly beneficial for sustained energy and prolonged satiety. Taken together, understanding the food matrix's impact on nutrient bioavailability is crucial for optimizing dietary strategies. Whether consuming SP for muscle recovery, gut health, or overall nutrition, considering its interactions within a meal can enhance its benefits.

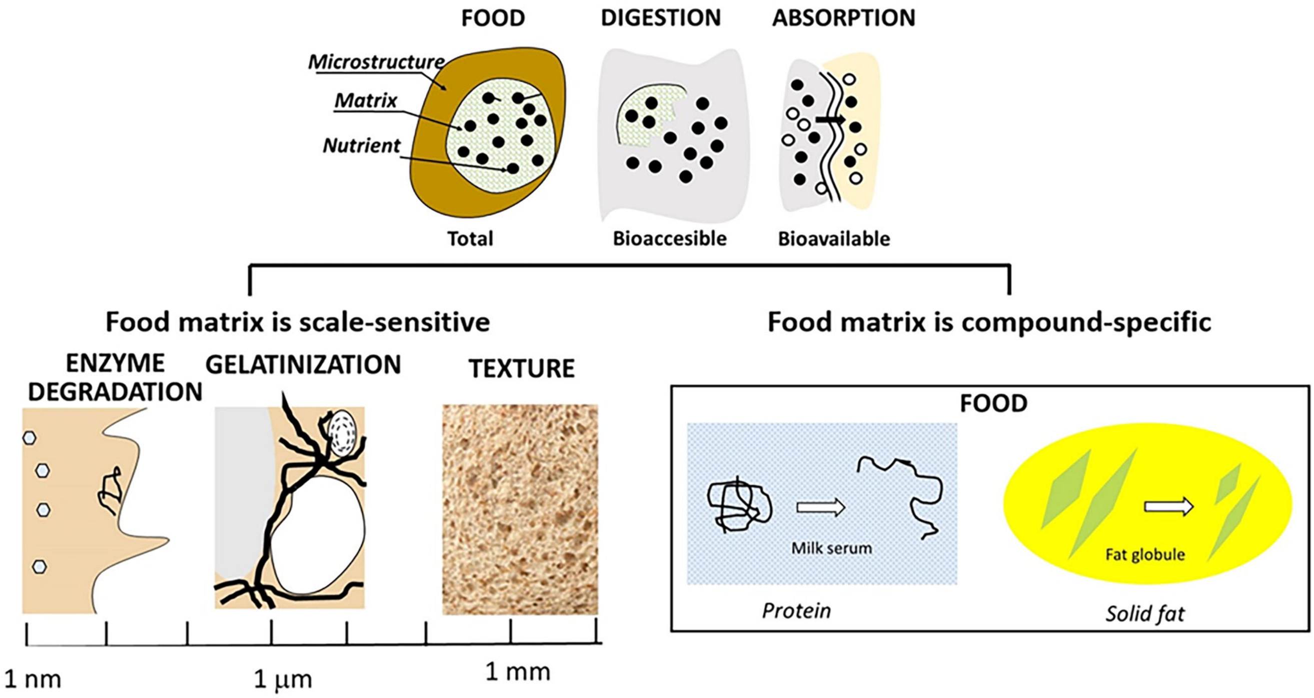


**FIGURE 1** | Simplified scheme illustrating the role of the food matrix in bioaccessibility and bioavailability, highlighting scale-sensitivity in bread (bottom left) and compound-specificity in milk (bottom right). *Source:* Withdrawn from Aguilera (2019).

### 5.3 | Textural Properties

Food texture is primarily determined by the macromolecular content of the ingredients. Especially, proteins exhibit gelation, water and fat retention, emulsification, foaming, and dough conditioning properties, which make them favorable for food processing. SP is widely used in the food industry due to its technofunctional features, like texture enhancement and nutritional enrichment of processed foods. As the presence of several ANFs reduced its popularity in Western countries, continuous efforts are made to explore effective processing methods to inactivate these factors and benefit from utilizing SP as a functional ingredient and desirable substitute (Haidar et al. 2018). SPI, SPC, and textured SP are the three major SbF with varying protein content and structure. Textured SPs derived from defatted soy flour are commonly used as meat alternatives to produce vegetarian/vegan burgers and sausages through their fibrous texture mimicking meat proteins (Kyriakopoulou et al. 2021). High protein and fiber content, nutritional quality, and sustainable production favor the use of SbF as meat analogs. On the basis of the mentioned functional properties, SP is considered a desirable ingredient of processed meat products as well (Kausar et al. 2019; Rubio et al. 2020). For instance, incorporating SPs as meat extenders increases cohesiveness to provide textural stability and enhances taste and appearance, nutrient profile, and formulation cost (Kyriakopoulou et al. 2019). Soy-based milk and yogurt mainly contain SP and are desirable PDPs to dairy foods (Plamada et al. 2023; Taeger and Thiele 2024). The remarkable water-holding capacity and nutritional content of SPs foster the use of soy flour in bakery products (Bianchi and Simonato 2025). Besides, breakfast cereals and relevant products enriched with SPI can present promoted functionality with improved protein content. Infant SbF are capable of serving as alternative protein sources in case of Cmilk sensitivity (Verduci et al. 2020).

SPs are highly considered in the preparation of conventional foods and home cooking for PDP-rich and well-textured products. For instance, heating triggers gelation of SP, enabling it to hold other ingredients and to generate a favorable texture in processed foods (Fu et al. 2023). Incorporation of SPs in baked foods improves bioactive content and texture due to moisture retention. High-protein bread and pasta, vegan (egg-free) cookies and cakes, alternative snacks, custards, and puddings are among the soy-based functional cooking suggestions (Navicha et al. 2018; Yano and Fu 2022).

## 6 | Influence of Processing Methods on SP Nutrition and Digestibility

Various treatments, such as heating, mechanical processing, enzymatic activity, and fermentation, can significantly affect the nutritional properties and digestibility of SP, as summarized in Table 5. Recent reports reviewed the influence of thermal, nonthermal, and bioprocessing on bioactivity and absorption of SP (Asghar et al. 2024; Kamiloglu et al. 2024; Lappi et al. 2022). Conventional cooking treatments, including boiling, roasting, and extrusion of SP, can inhibit ANFs and improve bioavailability of EAAs, leading to promoted $P_{Digest}$ (Kohli and Singha 2024). Most heat treatments, like autoclaving, are powerful processes to enhance the digestibility and nutritional quality of SPs while inactivating ANFs. Although heat-denatured SPs become susceptible to enzymatic digestion, excessive heat can cause protein aggregation, possibly lowering $P_{Digest}$ (Ton Nu et al. 2020). Extru-

**TABLE 5** | Recent reports evaluating the effect of various processes on nutritional properties and digestibility of soy proteins (SP).

| Soy protein/Soy food formulation | Process/Treatment | Application/Purpose | Nutritional properties | Digestibility/Absorptivity | References |
|---|---|---|---|---|---|
| Soybean meal (SM) | Solid-state fermentation (protease-enhanced *Streptomyces* sp.) | Improvement of nutritional value and protein digestibility ($P_{Digest}$) | Elimination of ANFs; increased bioactive nutrients | High soluble protein recovery (41%, w/w); improved digestibility (88.9%) | Lu et al. (2025) |
| Soy beverages | Four soy-based beverages: whole component, insoluble residue-removed, lipid-removed, and protein isolate containing | Comparison of $P_{Digest}$ | | $P_{Digest}$ ranged between 64.24% and 68.70%; the highest DIAAS values (96/80) and digestible protein (29.40/24.41 g/100 g of soybeans) were achieved by the whole component soy beverage | Zhao et al. (2025) |
| Soy sprouts (powdered) | Spray drying and heating after germination | Investigation of ANFs and $P_{Digest}$ | Decreased ANFs by 30%–60%; proper germination and heating improved nutritional value | Increased $P_{Digest}$ through germination by 5.88% difference from non-germination group | X. Wang et al. (2025) |
| SP | Fermentation (*Bacillus subtilis*) | Evaluation of nutritional quality and functionality | 48 h fermentation enhanced the nutritional, functional, and sensorial quality of SP | Increased soluble protein content and hydrolyzates, improving $P_{Digest}$ | Gao et al. (2024) |
| SM | Enzymolysis (complex enzymes)-fermentation (*Lactobacillus plantarum*) | Improvement of growth performance and nutrient digestibility | Increased content of soluble protein, peptides, and total free AAs by 261.75%, 300.00%, and 164.24%, respectively, while reducing ANFs | Improved digestibility | Cheng et al. (2024) |
| Soybean products (douchi, natto, doujiang, furu, and soybean yogurt) | Fermentation (*B. subtilis, Aspergillus oryzae, Mucor racemosus*, and *Lactiplantibacillus plantarum*) | Comparison of nutritional composition, structure, and effects on gut microbiota | Significantly increased AA content and markedly decreased levels of ANFs after post-fermentation | Notable enhancement in gut microbiota and increased $P_{Digest}$ in correlation with the secondary structure modification | Miao et al. (2024) |
| Soy protein isolate (SPI) (mixed with zein) | Limited enzymatic (papain) hydrolysis | Improvement of functionality and digestibility | Remarkably elevated functional properties | Significantly increased digestibility after 30 min hydrolysis | D. Wu et al. (2024) |
| Soymilk and soybeans | Dry heating (160°C and 200°C) | Investigation of the role of protein aggregates on digestibility and bioactive content | Differed peptide composition and bioactivities of protein aggregates formed via different cooking methods | Formation of insoluble protein aggregates through heating; decreased $P_{Digest}$ upon increasing heating temperature | Zhang, Li, et al. (2023) |

(Continues)

TABLE 5 | (Continued)

| Soy protein/Soy food formulation | Process/Treatment | Application/Purpose | Nutritional properties | Digestibility/Absorptivity | References |
|---|---|---|---|---|---|
| Soybeans | High-pressure processing (5 and 10 min at 300, 450, and 600 MPa) and germination | Investigation of the impact on digestibility and anti-nutrient content | Reduced ANFs and increased free AA release | Enhanced protein bioaccessibility and improved digestion | X. Wu et al. (2023) |
| Soy burger | Pan cooking | Comparison to meat-based burgers | Comparable protein quality and integrity | Good $P_{Digest}$ from 55% to 40% | Cutroneo et al. (2023) |
| SM | Double-stage fermentation (*A. oryzae* and *B. subtilis*) | Investigation of impact on digestibility and performance in broiler feeding | Higher protein content and total essential, nonessential, and free AAs; improved growth performance | Improved nutrient absorption and $P_{Digest}$ | Abdel-Raheem et al. (2023) |
| Soy protein concentrate (SPC) and SM | Enzyme treatment and fermentation (*Lactobacillus* and *Bacillus*) | Comparison on growth performance and functionality | Partially favored growth performance; contributed to an increase in immune response due to induced allergenicity | No significant effect on intestinal health | Deng et al. (2023) |
| SM | Fermentation | Evaluation of digestibility | | Provided highly digestible AAs and improved digestibility varying within 83% and 88% | Jang and Kim (2022) |
| SPI | Atmospheric cold plasma (170, 200, and 230 V, at time intervals of 5, 10, and 15 min) | Evaluation of the structure and functionality | Reduced ANFs, structural modification, improved protein solubility, and WHC, leading to better product quality | Enhancement (3.4-fold) of $P_{Digest}$ | Dabade et al. (2023) |
| SM | Fermentation (mixed culture of *B. subtilis, Aspergillus niger, Saccharomyces cerevisiae*, and *L. plantarum*) | Evaluation of the nutritional value | Increased content of protein, essential AAs, and macro- and micronutrients while decreasing ANFs | Increased easily digestible protein and amine nitrogen | Sukhikh et al. (2022) |
| | Fermentation (mixed culture of *B. subtilis*, *Lactobacillus*, and yeast) | Investigation of nutrient digestibility and intestinal functionality | Increased nutrients while decreasing ANFs | Better digestibility of CP and AAs, highly correlated with the enhanced activities of digestive enzymes and intestinal health | Yan et al. (2022) |
| SPI and soybean 7S fraction | Heat treatments (roasting and boiling) | Understanding of digestion resistance of SP fractions | | Digestion resistance through amyloid aggregates of 7S protein fraction; rapid protein hydrolysis via boiling, whereas no significant alteration in protein structure and digestibility via roasting | Han et al. (2022) |

(Continues)

**TABLE 5** | (Continued)

| Soy protein/Soy food formulation | Process/Treatment | Application/Purpose | Nutritional properties | Digestibility/Absorptivity | References |
|---|---|---|---|---|---|
| Soy waste (okara) | Enzymatic (protease) hydrolysis and fermentation (*L. plantarum*) | Improvement of nutritional and functional value of proteins | Higher degree of hydrolysis supported fermentation, revealing improved nutritional value and bioactivity | Improved digestibility and absorption; promoted release of polyphenols | R. Wang et al. (2022) |
| Black soybean | Fermentation and roasting (after germination) | Evaluation of the nutritional value and functionality | Declined ANFs and improved the nutritional quality and functionality | Increased solubility and enhanced digestibility and bioavailability | Chauhan et al. (2022) |
| SPI nanofibrils | Ultrasound (20 kHz, 750 W, with amplitudes of 20%, 40%, 60%, and 80% with a pulse duration of 5 s on/5 s off) | Investigation of structure, functionality, and digestibility | Altered structure, functional features, and bioactivity via applied amplitudes | Significantly enhanced digestibility at high amplitudes | Hu and Li (2022) |
| Soybeans | Heat treatments at different moisture contents | Investigation of molecular structure and digestibility | Heat denaturation induced protein aggregates and oxidation and decreased solubility | Mild oxidation and non-covalent aggregation increased $P_{Digest}$, whereas rising oxidation decreased $P_{Digest}$ | J. Zhang et al. (2022) |
| SPC | Boiling (100°C for 30, 90, and 180 min) (after germination) | Evaluation of structural changes relevant to digestibility | Induced distinct changes in physicochemical properties and secondary structure of proteins | Increased $P_{Digest}$ in germinated soybean; limited increase in digestibility upon boiling period | Zahir et al. (2021) |
| Soybeans | Soaking, boiling, and fermentation | Comparison of $P_{Digest}$ via applied treatments | Improved nutritional values, bioavailability of AAs, and certain bioactivities, especially via fermentation | Significantly increased $P_{Digest}$ via boiling and fermentation | Ketnawa and Ogawa (2021) |
| Tofu/Soya milk | Freeze-drying/UHT | Comparison of nutritional quality and $P_{Digest}$ | Desirable nutritional protein quality due to well-balanced AAs | High $P_{Digest}$ | Reynaud et al. (2021) |
| Soy milk and soy yogurt | Lactic acid fermentation (*L. plantarum*) | Investigation of gastrointestinal $P_{Digest}$ | | Different digestion patterns resulted in different peptide contents and altered gut microbiota for the given SbF | Z. Zhang et al. (2021) |
| SP | Ultrasonication (20 kHz, 750 W, with amplitudes of 20%–40% for 10–20 min) | Evaluation of the structure, functionality, and digestibility | Optimized restructuring at 30% amplitude and 10 min; improved functional features | Significantly increased (12.4%) $P_{Digest}$ due to bioavailability of exposure functional groups | Khatkar et al. (2020) |

(Continues)

**TABLE 5** | (Continued)

| Soy protein/Soy food formulation | Process/Treatment | Application/Purpose | Nutritional properties | Digestibility/Absorptivity | References |
|---|---|---|---|---|---|
| Soybeans | Combined boiling (100°C for 3.5 h) and fermentation (*S. cerevisiae*) | Evaluation of the cell porosity and digestibility | Inactivation of trypsin inhibitors | Increased cell permeability to trypsin contributed to increased $P_{Digest}$ | Zahir et al. (2020) |
| | Pressure cooking and fermentation (*B. subtilis* var. *natto*) | Evaluation of $P_{Digest}$ | Remarkably increased essential AAs and antioxidant activity, contributing to higher nutritional value | Improved $P_{Digest}$ of cooked soybeans by 45% | Ketnawa and Ogawa (2019) |
| SM | Enzymatic treatment and fermentation | Comparison with other treatments for growth performance, nutrient digestibility, and bioactivity | Enzyme-treated soy improved the growth performance, immune function, and antioxidant capacity | Similar apparent total tract digestibility of nutrients for enzyme-treated and fermented SbF | Ma et al. (2019) |

Abbreviations: AA, amino acid; ANF, anti-nutritional factor; CP: crude protein; DIAAS, dietary indispensable amino acids.

sion cooking can lead to mechanical degradation and structural modification of SP and a reduction of some ANFs, resulting in increased $P_{Digest}$ and improved nutritional quality (Hemetsberger et al. 2022). Blending SP with other proteins, like milk protein concentrate, can also elevate $P_{Digest}$ (Khalesi and FitzGerald 2021).

Enzymatic treatment digests SP, revealing various-sized peptide fragments with improved $P_{Digest}$. When compared to the other processing methods, fermentation plays a crucial role in the modification of the structure, nutritional facts, and functionality of SP (Emkani et al. 2022). *Lactobacillus plantarum*, *Bacillus subtilis*, and *Saccharomyces cerevisiae* are some common microorganisms used for soy fermentation. Fermentation can lead to inactivation of trypsin inhibitors, phytates, and lectins, which can limit $P_{Digest}$ and nutrient bioavailability. Germination and fermentation can disturb the integrity of cotyledon cells and induce permeability of the cell walls for the passage of digestive enzymes (Zahir et al. 2020). Complex protein structure is broken down and becomes accessible for digestion through the fermentation process. Thereby, $P_{Digest}$ and nutrient absorption can be elevated. Tempeh, miso, tofu, and natto are the traditional Asian fermented soy products and have higher $P_{Digest}$ in comparison to unfermented soy (do Prado et al. 2022). Heating and other processing treatments affect the nutritional quality and functionality of fermented soy products (Huang et al. 2022). Evidence indicated that microbial fermentation increased beneficial metabolites while degrading ANFs, which improved the nutritional value and functionality of soybean meal, making it a favorable feed for animals (Xue et al. 2024). Cross-linking of proteins with ANFs is limited through fermentation as well, facilitating the susceptibility of proteins to digestive enzymes (Ma et al. 2018).

On the other hand, fermentation increases the bioavailability of soy isoflavones by breaking down complex compounds into more easily absorbable forms. Fermented soy products, such as tempeh and miso, had higher isoflavone bioavailability compared to non-fermented soy (Rizzo 2024; Tamang et al. 2021). The isoflavones are linked to health benefits such as reduced cancer risk and improved cardiovascular health (do Prado et al. 2022). Fermentation also reduces ANFs like phytates and tannins, which otherwise inhibit nutrient absorption (Deng and Kim 2024). Fermentation enhances protein digestibility (reaching up to 92.7% for tofu compared to 65.3% for steamed beans) and degrades flatulence-causing oligosaccharides (Qin et al. 2022). Fermentation also increases isoflavone aglycone content and significantly improves mineral bioavailability by degrading phytate complexes that would otherwise bind to minerals like iron and zinc in the gut (Harahap et al. 2025). Conversely, isolation and concentration processes, such as those used for SPI, effectively remove indigestible carbohydrates and ANFs, resulting in a high protein content with digestibility of 93%–97% (van den Berg et al. 2022).

Other processing methods, including heat treatment and enzymatic hydrolysis, also affect SP bioavailability. A review by van den Berg et al. (2022) highlighted how different processing techniques influence protein quality, as measured by DIAAS and PDCAAS. Optimizing these methods can enhance the nutritional quality of SP products. Heat processing, such as toasting or extrusion, improves protein digestibility ($P_{Digest}$) by denaturing trypsin inhibitors and lectins; however, excessive heat can trigger Maillard reactions, reducing the bioavailability of EAAs like lysine (Takács et al. 2022; van den Berg et al. 2022; Ke et al. 2024). Alkalization, often employed in SPI production, adjusts pH to remove oligosaccharides but may concurrently alter protein structure (Harahap et al. 2025).

## 7 | Cultural, Dietary, and Safety Contexts

### 7.1 | Cultural and Dietary Integration of SP

SP has been a dietary cornerstone in many cultures for millennia, particularly in East Asia, where it is consumed in diverse forms such as tofu, tempeh, miso, natto, and soy milk. Traditional Asian diets incorporate these soy products as primary protein sources, often in fermented forms that enhance digestibility and nutrient bioavailability (Qin et al. 2022). In contrast, Western dietary patterns have historically included SP in more processed formats, such as textured vegetable protein in meat analogs, protein bars, and fortified foods. However, the growing demand for plant-based diets has led to increased global soy consumption, driven by its nutritional benefits and sustainability advantages over AnPr (Yan et al. 2024). The nutritional profile of soy—high in EAAs, fiber, and bioactives like isoflavones—makes it a valuable alternative to AnPr, particularly in vegetarian and vegan diets (Rizzo and Baroni 2018). Despite its benefits, cultural acceptance varies, with some populations preferring traditional soy preparations over processed SPI due to taste, texture, and perceived naturalness (Aiking and de Boer 2020).

### 7.2 | Environmental Impact and Safety of SP

The environmental benefits of SP compared to AnPr are well-documented. Life cycle assessments (LCAs) indicate that soy production requires significantly less water, land, and energy while generating fewer greenhouse gas emissions than beef, pork, or poultry production (Poore and Nemecek 2018). For instance, SPI has a carbon footprint approximately 10 times lower than beef protein/g (Clune et al. 2017). However, sustainability concerns arise from large-scale monocropping, particularly in South America, where soybean cultivation has been linked to deforestation and biodiversity loss (de L. T. Oliveira 2021). Sustainable sourcing initiatives, such as the Roundtable on Responsible Soy (RTRS), aim to mitigate these impacts by promoting agroecological practices and zero-deforestation commitments (Gasparri et al. 2013, 2016). Compared to livestock farming, soy remains an environmentally favorable protein source, especially when produced under regenerative agricultural systems.

Soy allergy is among the most common food allergies in infants and young children, with an estimated prevalence of 0.4%–1.0% (Taylor et al. 2021). Most reactions are mild-to-moderate, including atopic dermatitis, GI distress, or oral allergy syndrome, though severe anaphylaxis is rare. Infant SbF are frequently used as an alternative for infants with CMPA, but up to 10%–14% of these infants may also react to SP (Mousan and Kamat 2016). Consequently, guidelines from AAP and ESPGHAN recommend extensively hydrolyzed or AA-based formulas for infants with confirmed soy allergy (Vandenplas et al. 2024). Soy isoflavones, particularly genistein and daidzein, are phytoestrogens that can bind to estrogen receptors, raising concerns about potential endocrine effects in infants, children, and hormonally sensitive populations (Kim 2021). However, extensive reviews by EFSA and the US National Toxicology Program (NTP) conclude that isoflavone exposure from infant SbF (typically <3 mg/kg body weight/day) does not adversely affect growth, development, or reproductive health (EFSA Panel on Genetically Modified Organisms (GMO) 2015; Suarez-Torres et al. 2020). For adults, epidemiological studies suggest that moderate soy consumption (25–50 g/day of SP or 30–100 mg/day of isoflavones) is safe and may even confer health benefits, such as reduced cardiovascular risk and improved bone health (Messina, Duncan, et al. 2022; Messina, Mejia, et al. 2022). However, excessive supplementation (>150 mg isoflavones/day) in postmenopausal women has been debated for potential estrogenic effects, though clinical evidence remains inconclusive (Křížová et al. 2019).

SP is a culturally significant, nutritionally dense, and environmentally sustainable protein source with a well-established role in global diets. Although soy allergies in infants require careful management, and isoflavone intake should be moderated in specific populations, current evidence supports its safety within recommended consumption levels. Optimization of processing techniques to minimize allergenicity and further clarification of the long-term effects of isoflavones in sensitive subgroups is warranted. The International Agency for Research on Cancer (IARC) has never released a specific monograph evaluating soy, soy isoflavones, genistein, or daidzein for evidence of carcinogenicity. The search results demonstrate that IARC references appear in a variety of scientific literature, noting various IARC Monographs on other substances (such as chemical carcinogens), but there is no reference regarding a dedicated evaluation by IARC on soy. The IARC Monographs Programme considers environmental factors as potential human carcinogenic hazards, but soy and its isoflavones do not appear to have had a formal assessment (AICR 2021).

## 8 | Future Research Priorities and Clinical Implications

Methodological factors show that study design factors explain significantly more variance in effects than population factors. Studies showing positive effects share similar features: enough length, usually >6 months; the right dose under whole foods or isolated compounds; and outcomes including a biomarker to ensure biological activity (Asbaghi et al. 2020; Oliveira et al. 2021; Reed et al. 2021; Sepandi et al. 2022). The largest research gap is no studies looking at how best to integrate SPs into overall dietary patterns. Most studies have treated soy as an isolated variable, likely oblivious to any synergistic and antagonistic interactions with a variety of dietary components. To bridge the gap, studies would adopt a food systems perspective to evaluate the quality of diet as it pertains to soy consumption. Personalized nutrition is the next frontier for soy research, as genetic polymorphisms associated with estrogen receptors, isoflavone metabolism enzymes, and inflammatory pathways contribute to high inter-individual variability in the response to soy. Population-based recommendations should shift toward personalized nutrition recommendations based on genetics, metabolism, and lifestyle.

### 8.1 | Soy-Mediated Health Effects: A Life-Span Perspective

The health effects of SPs are mediated through their phytoestrogen content, particularly genistein and daidzein, through a selective estrogen receptor modulator effect. These compounds show tissue-specific effects that vary dramatically through the stages of life, which explains the often-contrasting results regarding soy consumption and health (Canivenc-Lavier and Bennetau-Pelissero 2023; Tibenda et al. 2022). Multiple lines of evidence from mechanistic work indicate that phytoestrogens preferentially bind to estrogen receptor $\beta$ (ER$\beta$) rather than estrogen receptor $\alpha$ (ER$\alpha$), with a binding affinity approximately 100–1000-fold lower than endogenous estradiol (Ionescu et al. 2021; Malik et al. 2023). This pattern of selectivity explains how soy compounds can produce estrogenic effects simultaneously in physiologically estrogen-deficient postmenopausal women while being antiestrogenic in high-estrogen premenopausal women and developing infants (Li et al. 2023). A critical synthesis of dose-response findings shows a biphasic dose-response relationship, consistently finding positive effects at dietary consumption levels of soy foods containing one to three servings daily, or 25–50 mg isoflavones, with limited or negative effects for higher pharmacological dosage levels at 100 mg isoflavones and above (Jodynis-liebert and Kujawska 2020). This pattern is observed for all outcomes across cardiovascular effects, bone health, and cancer prevention and suggests that pathways in soy/soy isoflavone research reliant on dose-response are better understood through the frames of therapeutic window or phase response than dose-response (Ferriere et al. 2024).

Developmental timing appears to be an important moderator of soy effects and responses. Meta-analyses of studies examining early exposure during infancy or childhood versus adult soy consumption showed opposite or fundamentally different response profiles. Early-life exposure appears to program protective long-term responses through epigenetic means, whereas exposure as an adult is protective but likely short-term through direct receptor signaling (Aboushanab et al. 2022). In addition to their estrogenic mechanisms, SPs have repeatable anti-inflammatory and metabolic effects that span traditional organ system boundaries. Several meta-analyses of biomarker studies discovered a common inflammatory signature of significant reductions in C-reactive protein, interleukin 6, and TNF-$\alpha$ across various populations (Asbaghi et al. 2020; Gholami et al. 2022). This inflammatory modulation provides a mechanistic explanation linking disparate health outcomes. The cardiovascular benefits seen in postmenopausal women, the cancer risk reduction in Asian populations, and the increased bone density in older individuals all derive from this active anti-inflammatory pathway. Studies that have failed to show benefits included long-term studies that reported beneficial effects in populations with low baseline inflammation and/or studies that were short enough to limit additional systemic effects (Prokopidis et al. 2023). Metabolic profiling studies completed via proteomics and metabolomics report a consistent soy signature with improved insulin sensitivity, enhanced lipid metabolism, and better AA utilization. This signature was strongest in the metabolically compromised populations, such as diabetes, metabolic syndrome, and CVD, which explains why healthy populations show little or no detectable metabolic change following soy intervention (Ferriere et al. 2025; Mbachu et al. 2019; Zhang, Li et al. 2023).

### 8.2 | Risk-Benefit Profiles Across Vulnerable Populations

A thorough synthesis of safety data from a number of studies indicates that concerns associated with SbF feeding have been fueled largely by methodological issues and inappropriate extrapolations from high-dose animal studies. The most significant insight from population-based studies is that safety must be considered within the context of nutritional adequacy and the appropriate comparator group (Vandenplas, Hegar, et al. 2021). From comparing three groups of fed infants, breast-fed infants, Cmilk formula-fed infants, and SbF-fed infants, the pattern continues to demonstrate that SbF perform the same as Cmilk formulas across neurodevelopmental, immunological, and reproductive outcomes, and both formula types perform slightly lower than breast-feeding. This pattern suggests that any theoretical risk associated with SbF must be judged against the known risks of inappropriate feeding alternatives (Andres et al. 2015; Maryniak et al. 2022; Verduci et al. 2020; Westmark 2017). Long-term follow-up studies demonstrated an important paradox: Countries exposed to high amounts of soy in early life under infants fed SbF during infancy possessed lower rates of hormone-sensitive cancers and CVD in adulthood. These data suggest that soy exposure in early life could confer long-term protective programming effects that result in greater benefits than any theoretical harm associated with the short-term risks (Messina, Mejia, et al. 2022; Qin et al. 2019; Sinai et al. 2019). Examinations of cancer epidemiology demonstrate a clear timing effect with soy use and hormone-sensitive cancers. In all situations, pre-diagnostic soy use—especially during adolescence and early adulthood—is associated with less breast cancer, whereas diagnostic—or subsequent soy consumption—appears to be either neutral or lead to a slight benefit (Sung et al. 2021; Xia et al. 2022). The timing effects also apply to other hormone-sensitive conditions. For menopausal symptoms, soy isoflavones show their maximal effect if initiated during the menopausal transition versus after a woman has fully transitioned into menopause. For prostate health, consumption of soy over their lifetime rather than starting in midlife shows greater protective effects (Ho et al. 2021; Ma et al. 2023). The mechanism that underlies these timing effects is likely due to an interaction between receptor expression changes by tissue specificity across our lifetime, along with epigenetic programming that occurs during particular development windows. This is why studies that use adult-onset, short-term interventions often fail to replicate the protective effects seen in the epidemiological studies that included longevity of soy consumption.

## 9 | Conclusions

SP has long been a subject of both interest and debate within the fields of nutrition and health. This review revisited the nutritional composition, digestibility, functional benefits, and safety profile of SP for both infants and adults. The collective evidence supports that SP is a high-quality PDP source with a complete AA profile and favorable bioavailability. In infants, SbF remain a safe and nutritionally adequate alternative to dairy-based options, particularly for those with lactose intolerance or CMPA, although they are not recommended for preterm infants due to concerns about mineral absorption and phytoestrogen exposure. In adults, SP has demonstrated benefits in supporting muscle maintenance, cardiovascular health, and metabolic regulation while also contributing to environmentally sustainable dietary practices.

Despite past controversies, particularly regarding isoflavones and hormonal effects, current data have not substantiated significant adverse outcomes when soy is consumed in typical dietary amounts. Nevertheless, population-specific research and long-term studies remain important for refining dietary guidelines and addressing ongoing concerns. As global demand for sustainable protein sources continues to rise, SP stands out not only for its nutritional adequacy but also for its versatility in food applications. Future research should continue to focus on optimizing SbF, improving palatability, and expanding its functional uses across age groups and health conditions. Embracing SP as part of a balanced diet offers a promising path toward improved health outcomes and greater dietary diversity.

## Author Contributions

**Tolulope Joshua Ashaolu**: conceptualization, writing – original draft, visualization, writing – review and editing. **Chi-Ching Lee**: writing – original draft. **Ozgur Tarhan**: writing – original draft. **Ali Rashidinejad**: writing – original draft, visualization. **Seid Mahdi Jafari**: writing – review and editing.


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The authors have nothing to report.

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The authors declare no conflicts of interest.

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