Naturally occurring hormones in foods and potential health effects

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Abstract
Hormones and hormone-like substances, for example, phytoestrogens, are food components that can be endogenously produced by a food source or occur secondary to farming practices. The hormone content of foods has been studied for decades, and safety evaluations in the United States and Europe indicate that naturally occurring hormones found in foods are safe for human consumption. More recent studies have focused on the role of certain hormones found in specific foods (e.g. dairy or soy) and their potential health effects. However, limited summaries exist on food content of hormones and hormone-like phytoestrogens in the context of a comprehensive US diet and implications, if any, of their daily consumption for overall health. This review provides an outline of hormone biosynthesis and functions in the body; discusses the more commonly studied, naturally occurring hormones in food and their biological role within food; estimates relative dietary contribution and when available, bioavailability, of naturally occurring food hormones; and summarizes the potential health associations of their intake in food. Based on the review of the scientific literature, the hormone content of typical serving sizes of commonly consumed foods is undetectable or in quantities that fall well within safety guidelines without any evidence for adverse effects on health.

Keywords
Hormones, steroid, estrogen, phytoestrogen, food safety

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Introduction
Crop foods as well as meat, fish, and other animal-based foods have been a staple of the human diet for thousands of years providing the essential nutrients for basic health.¹ As the population around the world grows, animal science experts have developed practices to efficiently grow animals and optimize food cultivation. One practice is the use of select hormones to support animal growth, feed efficiency, milk production, or animal health as a means to improve nutritional quality and/or food production efficiency.² Aside from agricultural practices, both animal and plant foods can contain endogenously produced hormones or hormone-like substances. Food cultivation, farming practices, and the resulting foods’ composition and content are continuously evaluated for food safety and health by regulatory groups, including the US Food and Drug Administration (FDA) and the Joint Food and Agriculture Organization and World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA).³–⁵ Despite the extensive regulation of the food supply from the farm to the table, concerns have been raised about the safety of hormones in foods and what effect, if any, they

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may have on human health.6,7 While hormone use in food cultivation is reviewed and managed by authoritative agencies, very few comprehensive scientific reviews are available for food science and nutrition professionals that summarize the naturally occurring hormone content in foods and its relationship to overall dietary intake, bioavailability, and general health. The aim of this review is to provide an overview of the types of naturally occurring hormones in foods and their biological roles within the food source; the relative dietary contribution and bioavailability of the more well-characterized hormones in foods; and the scientific literature on the key hormones and hormone-like substances as they are associated with health.

**Methods**

A search of the peer-reviewed scientific literature was conducted on PubMed using keywords, such as food hormones, hormone analysis of foods, hormone content of foods, food hormone biological role in food, bioavailability of naturally occurring food hormones, human health benefits of food hormones, plant foods, animal foods, analytical methodology of hormones in foods, measurements of hormones, and phytoestrogens in foods. Additional search terms included analysis of naturally occurring compounds, hormones, plant hormones, and phytochemicals in both plant and animal foods (e.g. dairy-milk products, eggs, fish, poultry, meat and pork). Abstracts of relevant articles published through May 2020 were accessed, reviewed, and summarized below.

**Hormones—A brief overview**

Hormones are a class of signaling molecules produced by glands in multicellular organisms that are transported by the circulatory system to organs to regulate physiology and behavior.8 They have key roles in the lifecycle during growth, development, and in reproduction of animals and for growth and immunity in plants.9 Hormones are endogenously produced throughout the lifecycle and can become an integral part of the structure of the animal or plant prior to becoming part of the food supply.9 Biosynthesis of human and animal hormones can be impacted by factors, such as diet (e.g. nutrient deficiency), genetics, and stress, while biosynthesis of plant hormones is also impacted by stressors, ultraviolet light, and climate variations.9–13 The majority of animal and plant hormones range in magnitudes of picogram to microgram levels, which are very low concentrations in comparison to other food components.9 For example, a food’s endogenous micronutrients (i.e. vitamins and minerals) range in the microgram to gram levels per serving.1

**Biological roles of hormones**

**Animal hormones**

Animals produce similar hormones to humans and thus animal-sourced foods common in the US diet, for example, dairy, meat, fish, and eggs, can contain hormones similar to those produced by humans. These hormones generally have the same biological roles and mechanisms of action within their native sources. A list of examples is provided in Table 1.

**Animal hormone-like substances found in plants**

Plant hormones are generally structurally and mechanistically different than animal hormones and encompass a broad group of compounds that are beyond the scope of this review. However, some commonly consumed plant foods, such as soy, nuts, seeds, and cereal grains, among others, contain substances that have hormone-like characteristics similar to the animal-based estrogens; these hormone-like substances are termed phytoestrogens.20 Phytoestrogens are one of the most studied hormone-like substances found in foods and include the isoflavones, ligands, coumestans, and certain classes of phytoalexins.21 All of these phytoestrogens play a role in normal development of the plant and in some cases, as protectants to environmental stressors.21 The phytoestrogens resemble the structure of estrogen and therefore have the capacity to bind to estrogen receptors (ERs) under certain circumstances or conditions, exerting both estrogen-like and antiestrogen properties.19,22 However, their binding affinity is substantially less than 17β-estradiol (E2), the most potent natural ligand of ERs.23 In fact, the estrogenicity of isoflavones is 4000–4,000,000 times lower than E223,24 For example, genistein and daidzein, found in soy, have a relative estrogenicity of 4.5 × 10⁻³ and 2.8 × 10⁻⁴, respectively, compared to E2 with an estrogenicity of 1.23,24 The binding affinity of isoflavones to ERs is also dependent on factors, such as life cycle stage, levels of endogenous estrogen, and levels of environmental estrogen-like compounds.25 The soy isoflavones are most well known for their ability to bind to ERα and ERβ. Soy isoflavones can preferentially bind to and transactivate ERβ and can mimic the effect of estrogen in some tissues and block its effects in other tissues.22,25 Aside from their known interactions with ERβ binding, isoflavones and their metabolites have biological activities that are unrelated to their interactions with ERs. For example, soy isoflavones can display anticancer properties through mechanisms, such as the inhibition of tyrosine kinase enzymes, which have a critical role in cell proliferation and can affect nuclear transcript factor-kappa B signaling, attenuating the inflammatory response.26,27

**Levels of select hormones and hormone-like substances found in common foods**

Reported levels of hormones and hormone-like substances in foods vary greatly within the peer-reviewed literature and are likely affected by endogenous production and assay methodology, making it challenging to compare levels between food sources from various publications. Within
the peer-reviewed scientific literature, two publications, though somewhat dated, provide among the most comprehensive estimations of levels of key steroid hormones and phytoestrogens in a wide range of commonly consumed foods. Recent literature has focused more on estrogens and phytoestrogens from specific food sources, particularly dairy. Therefore, while limitations may exist for estimating absolute hormone contents in foods from these studies, the relative amounts of hormones and hormone-like substances between foods can be assessed. Due to their comprehensive nature, their assessment of foods common in the Western diet, and their well-defined methodology, the data presented in these two publications were used to develop estimations of levels of select hormones or hormone-like substances found in 100 g portions (Table 2) or serving sizes (Table 3) of typical foods consumed in the United States. These estimations were compared to more recent literature on hormones and hormone-like compounds in specific foods and adjusted as necessary to reflect the most up-to-date data. However, given the high degree of variability of endogenously produced steroid hormones in animal foods and phytoestrogens in plant foods, levels presented should be interpreted with caution and are for informational purposes only with the aim of contextualizing and providing examples of levels that may theoretically be present in foods.

The lipophilic steroid hormones (Table 2) are found in the fat fraction of animal-based foods. For example, progesterone is more likely to be present in full-fat dairy foods and egg yolks compared to lower fat or fat-free foods, and estrogens, per 100 g, were more concentrated in eggs versus the other foods. Eggs likely contain estrogens since they are produced directly in the hen ovaries, a steroid-hormone synthesizing gland. Progesterone concentrations in milk, particularly the full-fat variety, likely reflect the variation of progesterone production and secretion during the lactation phases of the dairy cow.

Nut and oilsseeds contain the most phytoestrogens in the Western diet. Soy products, cereals and bread, legumes, meat products, soy-containing processed foods, vegetables, fruits, alcoholic and nonalcoholic beverages are also sources. Among specific phytoestrogens, soybeans and soybean products, followed by legumes, contain the highest concentrations of isoflavones, whereas lignans are the

| Hormones or hormone-like substance | Biological role within the original food source |
|-----------------------------------|-----------------------------------------------|
| IGF-I                             | Mediates growth hormone and promotes cell and organism growth |
| Growth hormone                    | Stimulates growth and cell reproduction; supports release of IGF-1 from liver |
| Insulin                           | Supports uptake of glucose, glycogenesis, glycolysis in liver and muscle |
| Prolactin                         | Supports release of breast milk |
| LH                                | Supports sexual maturation of ovarian follicles in females and spermatogenesis in males |
| Androgen                          | Stimulates growth of male sex organs and development of secondary male sex characteristics |
| Androstenedioid                   | Attenuates lipid accumulation in adipocytes and promotes the enlargement of myocytes |
| DHEA                              | Influences sex differences in behavior, anabolic |
| Testosterone                      | Supports anabolism including muscle development and strength, increases bone density |
| Estrogen                          | Stimulates growth and development of female sex organs |
| Estrone                           | Maintains health of blood vessels and skin |
| Estradiol                         | Reduces bone resorption |
| Progesterone                      | Regulates the endometrium of the uterus |
| Key regulator of critical steps in fetal development, including implantation and labor onset |
| Stimulates production of nutritive secretions during early stages of embryonic development |
| Promotes development of secretory apparatus of the mammary glands |
| Phytoestrogens                    | Establish symbiotic relationship between the soy plant root and rhizobial bacteria for formation of nitrogen-fixing root nodules |
| Genistein                         | Precursors to certain classes of phytoalexins that have a role in normal development as well as protectants to many environmental stresses |
| Daidzein                          | Protects the plant from external stresses such as fungi |

DHEA: dehydroepiandrosterone; FSH: follicle-stimulating hormone; IGF-1: insulin-like growth factor-1; LH: luteinizing hormone. Sources: Shigenaga and Argueso, Patra et al., Grosvenor et al., Fritsche and Steinhart, Galbraith, Scanes et al., Scarth et al., Dixon, Thompson et al., and Yu et al.
primary sources of phytoestrogens found in nuts and oilseeds. Lignans are also found in cereals, fruits, and vegetables, and coumestans are found in peas, beans, alfalfa, and clover sprouts. As noted, phytoestrogen content varies significantly among foods and within the same group of foods depending on growth, environmental conditions, and processing methods.

Theoretical amounts of naturally occurring hormones that may be consumed within a standard 2000 calorie meal plan using recommendations from each food group and/or subgroup in the 2015 Dietary Guidelines for Americans are provided in Table 4. The estimations in this table are based on serving size calculations in Table 3. Using these estimations, higher amounts of phytoestrogens versus the other assessed hormones are available in the diet. The main source of phytoestrogens comes from foods in the protein group due to the inclusion of soy in the protein-based legumes category. Foods in the dairy, protein, and oils/fats groups are estimated to be the main sources of progesterone. Dairy and protein group foods are estimated to be the major contributors of animal-based estrogens.

Regardless of whether a food is a major contributor, the overall hormone content of foods is negligible compared to the amounts reported to be produced within the body (Table 4); for example, according to one study, the intake of three servings/day of milk is estimated to contain roughly 0.01–0.1% of the total daily estrogen production in women. It is important to note that the total daily estrogen production rate to be 9110 ± 1110 μg/day in young, healthy, white males and 7220 ± 1150 μg/day in young, healthy, Asian males; however, the circulating concentrations in the same set of subjects ranged from 0.003 μg/mL to 0.010 μg/mL. Steroid hormones are constantly being produced and metabolized, and there is significant variation in the production and metabolic rates and the circulating levels within each person; episodic fluctuations, daily diurnal rhythm, menstrual cycle phase, age, sleep, illness, and physical activity are just some of the factors that affect levels. Phytoestrogens can be present in foods in much greater quantities, hundreds to thousands of times the concentrations of endogenous estrogens, but they are significantly less potent than endogenously produced estrogens and bind less tightly to steroid hormone serum transport proteins than endogenous estrogens.

In addition to steroid hormones or hormone-like substances found in foods, certain exogenous hormones can boost the production of milk and/or meat in animals. These hormones are provided to the animal for food production purposes. For example, recombinant bovine growth hormone (rBST) can be used to boost milk production in the dairy industry. The FDA provides strict guidance and details on careful use, administration, and dosage limits of hormone usage in dairy cattle. In the case of rBST, the FDA approved the use of rBST for milk production after it critically examined the safety of milk from treated cows and confirmed that the drug does not harm treated animals or the environment. Research shows that administering rBST to cows does not alter milk composition or nutritional quality. Furthermore, because rBST is a protein, its consumption proceeds like any other ingested protein in humans: it is degraded into its amino acid constituents, is

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**Table 2. Levels of hormones or hormone-like substances found in common foods (μg/100 g).**

| Food                  | Testosterone | DHEA  | Androstenedione | Progesterone | Estrogens | Total steroid hormones | Phytoestrogens |
|-----------------------|--------------|-------|-----------------|--------------|-----------|------------------------|---------------|
| Butter                | <0.005       | 0.115 | 0.598           | 14.1         | 0.029     | 14.8                   | 1113          |
| Cereals and breads    |              |       |                 |              |           |                        |               |
| Chicken               | <0.0004–0.003| <0.002| <0.002          | 0.023        | 0.0004–0.005| 0.008–0.028             | 73            |
| Eggs                  | 0.004–0.19   | 0.005–0.176| 0.183–0.927 | 1.25–4.36   | n.d.–0.14 | 1.44–5.79               |               |
| Fish (herring, carp)  | <0.002–0.007 | 0.016–0.06 | 0.003–0.029 | <0.01–0.051| <0.005    | 0.036–0.147             |               |
| Fruits                |              |       |                 |              |           |                        |               |
| Ham                   | 0.004–0.005  | 0.024–0.064| 0.009–0.039 | 0.096–0.151| <0.005    | 0.138–0.259             | 2.3           |
| Legumes (nonsoy)      |              |       |                 |              |           |                        | 504           |
| Meat/beef             | <0.002–0.4   | 0.01–0.09| 0.02–0.08 | 0.01–2.15  | <0.005    | 0.047–2.72              |               |
| Milk                  | <0.001–0.009 | 0.013 | 0.211           | 0.981–1.21  | 0.004–0.015| 1.03–1.26              | 0.5–1.2       |
| Nuts and seeds*       |              |       |                 |              |           |                        | 32403         |
| Potatoes (white)      | <0.002       | 0.0399| 0.005           | 0.507       | <0.005    | 0.550                  | 1.4           |
| Soybeans/products     | <0.005       | 0.031 | <0.005          | <0.03       | <0.012    | 0.083                  | 19837         |
| Turkey                | <0.0004–0.0023| 0.005| 0.006           | 0.818       | 0.0004–0.003| 0.005–0.083             |               |
| Wheat*                | 0.009–0.019  | 0.015–0.067| 0.01–0.048 | 0.06–0.286 | <0.012    | 0.106–0.420             | 9.8           |
| Vegetables            | <1–100       |       |                 |              |           |                        |               |
| Yogurt                | <0.001       | 0.011 | 0.056           | 1.33        | 0.018     | 1.42                   |               |
| Oil (olive)           | 0.002        | 0.004 | 0.002           | 0.008       | 0.005     | 0.021                   | 180.7         |

*Phytoestrogen content is provided for nuts, seeds, and oils and progesterone, testosterone and estrogens contents are provided as the sum found in olive, safflower, and corn oils.

*Phytoestrogen content is for wheat bread and progesterone, testosterone, and estrogens contents are provided for wheat.

Sources: Thompson et al., Hartmann et al., Di Gioia and Petropoulos, Malekinejad et al., and Norskov et al.

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**Sources:** Thompson et al., Hartmann et al., Di Gioia and Petropoulos, Malekinejad et al., and Norskov et al.
Table 3. Levels of hormones or hormone-like substances found in common foods (μg/serving size).

| Food (serving size)           | Testosterone | DHEA     | Androstenedione | Progesterone | Estrogens | Total steroid hormones | Phytoestrogens |
|------------------------------|--------------|----------|-----------------|--------------|-----------|------------------------|---------------|
| Butter (1 tbsp)              | <0.0007      | 0.0163   | 0.0849          | 2.0022       | 0.0041    | 2.1                    | 445.2         |
| Cereals and breads (40 g)    |              |          |                 |              |           |                        |               |
| Chicken (3 oz)               | <0.0003–0.026| 0.0000–0.0017| 0.0000–0.0017  | 0.0000–0.0196| 0.0003–0.0043| 0.007–0.024            |               |
| Eggs (50 g)                  | 0.0020–0.095 | 0.0025–0.0880| 0.0915–0.4635  | 0.6250–2.18  | n.d.–0.07 | 0.721–2.90             |               |
| Fish (herring, carp) (3 oz)  | <0.0017–0.0060| 0.0136–0.0510| 0.0026–0.0247  | <0.0085–0.0434| <0.0043  | 0.031–0.125            |               |
| Fruits (140 g)               | 0.0034–0.0043| 0.0204–0.0544| 0.0077–0.0332  | 0.816–0.1284 | <0.0043  | 0.117–0.220            | 1.955         |
| Ham (3 oz)                   |              |          |                 |              |           |                        | 453.6         |
| Legumes (nonsoy) (90 g)      |              |          |                 |              |           |                        |               |
| Meat/beef (3 oz)             | <0.0017–0.3400| 0.085–0.0765| 0.0170–0.0680  | 0.0085–1.8275| <0.0043  | 0.040–2.31             |               |
| Milk (1 cup)                 | <0.0024–0.0220| 0.0317   | 0.0512          | 2.3936–2.9280| 0.009–0.0366| 2.52–2.95              | 1.22–2.928 |
| Nuts and seedsa               |              |          |                 |              |           |                        | 9720.9        |
| (1 oz-eq)                    |              |          |                 |              |           |                        |               |
| Potatoes (1 medium)          | <0.0022      | 0.0340   | 0.0055          | 0.5577       | <0.0055  | 0.605                  | 1.54          |
| Soybeans/products (3 oz)     | <0.0043      | 0.0264   | <0.0043         | <0.0255      | <0.0102  | 0.071                  | 27543         |
| Turkey (3 oz)                | <0.0003–0.0020| 0.0043   | 0.0051          | 0.6953       | 0.0000–0.003| 0.002–0.705            |               |
| Wheatb (45 g)                | 0.0041–0.086 | 0.0068–0.0302| 0.0045–0.0216  | 0.0270–0.1287| <0.0054  | 0.048–0.189            | 4.41          |
| Vegetables (85 g)            |              |          |                 |              |           |                        | <1–85         |
| Yogurt (6 oz)                | <0.0017      | 0.0187   | 0.0952          | 2.261        | 0.0306   | 2.41                   |               |
| Oil (olive)                  | 0.00029      | 0.0057   | 0.00029         | 0.0011       | 0.00072  | 0.003                  |               |

*a*Phytoestrogen content is provided for nuts, seeds, oils and progesterone, testosterone, and estrogens contents are provided as the sum found in olive, safflower, and corn oils.

*b*Phytoestrogen content is for wheat bread and progesterone, testosterone, and estrogens contents are provided for wheat.

Sources: Thompson et al.20, Hartmann et al.28, Di Gioia and Petropoulos,30 Malekinejad et al.,31 and Norskov et al.32
Table 4. Naturally occurring hormone amount (μg) in foods (based on 2000 kcal diet) and endogenous daily production.

| Food (serving size) | Testosterone (μg) | DHEA (μg) | Androstenedione (μg) | Progesterone (μg) | Estrogens (μg) | Total steroid hormones (μg) | Phytoestrogens (μg) |
|---------------------|-------------------|-----------|----------------------|-------------------|----------------|-----------------------------|------------------|
| Fruit (2 c-eq)      | 0.008             | 0.116     | 0.0188               | 1.90              | 0.0188         | 2.06                        | 2195             |
| Vegetable (2.5 c-eq)| 0.015–0.032       | 0.025–0.113| 0.017–0.081          | 0.101–0.480       | 0.20           | 0.178–0.706                 | 1886             |
| Grains (6 oz-eq)    | 0.0048–0.047      | 0.115     | 0.37                 | 4.71–12.1         | 0.158          | 4.71–12.8                   | 5.76             |
| Dairy (3c-eq)       | 0.0197–0.7258     | 0.0847–0.6591 | 0.3311–1.6755      | 2.10–11.7         | 0.001–0.225     | 2.54–15.0                   | 99,801           |
| Proteins (5.5 oz-eq)| 0.0019            | 0.0321    | 0.162                | 3.81              | 0.009          | 4.01                        | 48.8             |
| Oils and fats (27 g)| 0.0019            | 0.0321    | 0.162                | 3.81              | 0.009          | 4.01                        | 48.8             |
| μg/day USDA healthy | Up to 0.0815      | Up to 1.035 | Up to 2.307          | Up to 30.013      | Up to 0.411     | Up to 34.6                   | 104,193          |
| eating plan (2000 kcal) |                 |           |                      |                   |               |                             |                  |

| Endogenous production levels | Testosterone (μg/day) | DHEA (μg/day) | Androstenedione (μg/day) | Progesterone (μg/day) | Estrogens (μg/day) | Total steroid hormones (μg/day) | Phytoestrogens (μg/day) |
|-------------------------------|-----------------------|---------------|--------------------------|-----------------------|---------------------|---------------------------------|-------------------------|
| Men                           | 5000–7000             | 4000 (young adults) | 3000                     | 750                   | 100                 | Up to 10,850                    | NA                      |
| Women                         | 100–400               | 4000 (young adults) | 1400–6200                | 2300–43,000 (premenopausal) | 70–720 (premenopausal) | Up to 44,920 (pregnancy) | NA                      |

DHEA: dehydroepiandrosterone.

Sources: Thompson et al.20, Hartmann et al.20, Hartmann et al.28, Baulieu,39 Feingold et al.40,41 Rochira et al.42 Golub et al.43 Siteri,44 Stanczyk,45 and USDHHS and USDA.46
rendered inactive, and undergoes regular absorption and/or nitrogen metabolism processes.\textsuperscript{4,51,52} As such, research indicates that rBST in milk does not have any physiological effect on humans.\textsuperscript{4,52}

In the case of meat production, estradiol, testosterone, and progesterone may be given to beef cattle in their feed to increase growth and development. As with milk production, there are strict safety guidelines and levels of use for these hormones in cattle for meat production.\textsuperscript{5} The FDA’s guidelines for safe consumption for these hormones is 1\% or less than the lowest amount produced by the human body each day,\textsuperscript{53} a safety limit far higher than the 0.01\% and 0.06\% that three servings of milk provide to the daily estrogen production in women and prepubertal boys, respectively.\textsuperscript{45,47} JECFA established an acceptable daily intake of 0–50 ng/kg body weight based on evaluation of the scientific studies; this range was established with two 10-fold safety factors (100-fold safety factor in total) to account for both individual variations and additional safety limits for sensitive populations.\textsuperscript{54} Thus, under the FAO/WHO guidelines, a 70 kg (154 lb) individual can consume up to 3.5 μg/day estrogen and still not reach the acceptable daily intake established by JECFA. Estimations in Table 4 show up to 0.411 μg/day intake of estrogen following a 2000 kcal diet. Also, according to the WHO,\textsuperscript{5} “people are not at risk from eating food from animals treated with these drugs (steroid hormones) because the amount of additional hormone following drug treatment is very small compared with the number of natural hormones that are normally found in the meat of untreated animals and that are naturally produced in the human body.”

Bioavailability

Few recent peer-reviewed publications address the bioavailability of steroid hormones when consumed in the diet. Prior research, which calculated the intake of steroid hormones in relation to human steroid production, concluded that endogenous human production far exceeds dietary intake levels and estimates suggest 90\% of the minute amount of ingested hormones are inactivated by the first-pass effect of the liver.\textsuperscript{28} This led to the conclusion that no hormonal effects can be expected from naturally occurring steroids in foods.\textsuperscript{28}

The bioavailability of isoflavones is dependent on the hydrolysis of their glycoside form to the aglycone.\textsuperscript{55,56} The β-glucosidases in the small intestine epithelial cells are responsible for hydrolysis of the glucose molecule to yield the form that can be absorbed.\textsuperscript{55,56} Absorption and bioavailability can vary among individuals and is related to differences in GI transit time, absorption, enterohepatic circulation, and metabolism by intestinal bacteria.\textsuperscript{55,56} Genistein is absorbed and then requires glucuronidation in the intestinal wall to convert this isoflavone to a more water-soluble metabolite that can circulate in the blood and be excreted in the urine.\textsuperscript{45,50} S-equol, the metabolite of the soy isoflavone daidzein, is produced by some people and may be dependent on the intestinal microflora, dietary habits, and individual genetics for this metabolic conversion.\textsuperscript{56–58} Isoflavones are typically excreted within a 24-h period after ingestion.\textsuperscript{57} Lignans, found in foods such as flaxseed, show a dose-response increase in both plasma and urine concentrations after intake.\textsuperscript{59}

Health effects

Estrogens and phytoestrogens

Limited peer-reviewed literature is available about health associations between estrogen intake from animal-based foods and health. Currently, both the FDA and WHO conclude that food consumption, which may contain naturally occurring estrogens (e.g. milk, fish, and so on), are safe for the daily diet. The USDA and WHO recommend intakes of these foods as part of a healthful dietary pattern to meet nutrient needs.\textsuperscript{46,60}

The health effect of soy phytoestrogens or isoflavones has been evaluated for over 25 years and continues to be studied in various populations. Isoflavone intake varies widely with the highest intake among Asian populations, where it ranges from about 10 to 15 mg/day in Hong Kong and 30–40 mg/day in Japan and Shanghai compared to about 3 mg/day in Western populations.\textsuperscript{22} Results from observational studies conducted among Asian populations indicate that higher intakes of soy foods are associated with reduced fracture risk and reduced cardiovascular disease risk.\textsuperscript{22} Interestingly, the relationship of soy intake and cardiovascular disease in Asian populations is observed in women but not in men.\textsuperscript{22} In addition to soy food intake, there are other hormonal differences between Asian and Western populations that may partially explain the reduced risk of chronic disease, such as later age of menarche, earlier age of menopause, and lower endogenous levels of sex hormones in Asian women.\textsuperscript{61} Unfortunately, there are few observational studies in Western populations due to the low intake of soy limiting the ability to provide meaningful data. Some observational studies on soy and cardiovascular disease in Western populations oversample vegetarians and other aspects of their diet and lifestyle may confound the effects of soy.\textsuperscript{22,62,63} Numerous clinical studies have shown a hypocholesterolemic effect of soy protein,\textsuperscript{22,64} suggesting that it may have an impact on risk factors for cardiovascular disease. Some studies have hypothesized that soy isoflavones may also be involved in reducing LDL cholesterol.\textsuperscript{65,66} Several meta-analyses of randomized controlled trials have consistently found a benefit of soy foods and soy protein for lowering LDL cholesterol, but the evidence for the benefit of soy isoflavones is mixed.\textsuperscript{65–69}

Phytoestrogens have also been investigated for their ability to modify breast cancer risk and manage menopausal symptoms. A recent meta-analysis of prospective cohort studies from Asian and Western countries found women

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with higher intakes of soy foods had reduced risk of developing breast cancer, consistent with previous meta-analyses. Several studies have also reported a benefit of genistein and equol (a byproduct of daidzein metabolism by large intestine bacteria) in the treatment of hot flashes and night sweats associated with menopause. The benefits of genistein have been seen at doses as low as 30 mg/day although the benefits seem to be greater in women with higher soy intake. Benefits of equol for hot flashes were seen at 10–30 mg/day according to a recent meta-analysis. Interestingly, around 70–80% of women in Europe and Latin America, where soy intake is lower, experience postmenopausal hot flashes, while only 20–25% of Asian women experience hot flashes.

Despite these potential health benefits, the estrogenic effect of soy isoflavones has also created concerns about their potential effect on pubertal development, fertility/reproduction, and male feminization. Earlier puberty in girls has been observed over the past several decades, particularly in Western countries, and this has coincided with an increase in the intake of soy foods. Yet, observational studies on isoflavone intake and pubertal timing are conflicting. Several cross-sectional and cohort studies have shown phytoestrogen exposure to be associated with delayed puberty in girls, while others have shown earlier pubertal maturation with phytoestrogen intake. The effect of phytoestrogens on pubertal timing in boys is not as well investigated, but a recent study in the United States found that moderate to high intake of soy isoflavones was associated with earlier age at pubarche in boys compared to boys with lower intake. However, the boys included in the study were from Seventh Day Adventist areas and schools to ensure a broader exposure to phytoestrogens. A recent study in the United States found that moderate to high intake of soy isoflavones was associated with earlier age at pubarche in boys compared to boys with lower intake. However, the boys included in the study were from Seventh Day Adventist areas and schools to ensure a broader exposure to phytoestrogens.

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**Insulin-like growth factor-1**

Insulin-like growth factor-1 (IGF-1) is a critical hormone involved in growth during childhood and anabolic responses, including maintaining muscle mass, in adulthood. Nutritional status throughout the lifecycle is highly linked to IGF-1 levels, with insufficient nutrition causing low IGF-1 circulating levels; however, in some reports, high concentrations of IGF-1 have been associated with the increased risk of prostate and premenopausal breast cancer. This link has raised health concerns about food intake that may increase IGF-1 blood concentrations. IGF-1 is a protein, and proteins are hydrolyzed into amino acids and absorbed during digestion, thus IGF-1 consumed in foods is not likely to raise IGF-1 blood concentrations. However, higher protein (and caloric) intake has been associated with increased IGF-1 levels. For example, results of a 2017 meta-analysis concluded that for each additional standard deviation of milk intake, there was a significant increase of 0.1 standard deviation in circulating levels of IGF-1. The odds ratio of prostate cancer risk was 1.09 (95% confidence interval: 1.03–1.16) with each standard deviation increase in circulating IGF-1. Similarly, soy protein intake at greater than 25 g/day intake is also associated with higher IGF-1 levels. Since IGF-1 levels are closely linked to nutritional status and protein intake, one explanation is that higher protein intake, per se, for example, regardless of whether the source is milk protein, soy protein, or any other protein, causes higher circulating IGF-1 levels. Since IGF-1 is sensitive to nutritional status, particularly protein intake, consumption of protein-containing foods likely increases IGF-1 to signal the body that it has resources (energy and protein) to allow for growth and maintenance. However, its significant involvement in growth may also be why it is linked to several cancer types. It is important to note that the association between protein intake, IGF-1, and cancer risk is not isolated, but rather, part of an integrated matrix of factors. For example, although milk intake has been shown to increase IGF-1, the World Cancer Research Foundation/American Institute of Cancer Research concludes in their recent Third Expert Report that there is strong evidence linking dairy product concentration or quality. A critical evaluation of the scientific evidence also showed no effect of soy isoflavones on male feminization. While two case studies of male feminization have been reported, the intake of soy isoflavones was 120 times the typical consumption and the men were also consuming unbalanced diets and may have had other nutrient deficiencies due to the extreme amount of soy foods in the diet. The preponderance of evidence to date has shown soy isoflavone intake, even up to 150 mg/day, and has no effect on circulating estrogen or testosterone levels. Ongoing work in the category of phytoestrogens and particularly soy isoflavones will provide additional understanding of health benefits.
intake to lower colorectal cancer risk.106 Given the complex and sensitive interplay between nutritional status, healthy growth and maintenance, and the deleterious growth of cancer cells, more research is needed to define the specific pathways of IGF-1, mechanisms of its control, and its downstream effects.

Conclusion
Hormones and hormone-like phytoestrogens occur naturally in the food supply and these hormones are required within the food source itself to ensure its own optimal growth and maintenance. Like the foods in which they are produced, these endogenous hormones and hormone-like substances have a long history of consumption and are considered safe by the food and ingredient regulatory agencies in the United States and around the world. A review of the existing data from scientific peer-reviewed literature shows animal foods that contain modest amounts of hormones, and of the hormones reviewed, progesterone and estrogens tend to be the most prominent among the naturally occurring hormones in animal-based foods. Yet, even these hormones are present in minute amounts well below the already conservative safety guidelines set by authoritative and regulatory agencies. Furthermore, the endogenous production of hormones and range in the human body is hundreds to thousands greater each day than the dietary intake levels available, without accounting for their reduced or absent bioavailability. Both progesterone and estrogens are lipid-soluble hormones, and several studies have shown that lower fat version of foods contains reduced levels of these hormones.28,29,31 Plant foods, such as soy, legumes, peas, oilseeds, and grains, contain phytoestrogens, which may have hormone-like activity with weak binding properties to ERs. The physiological and health effects of phytoestrogen intake are still an active area of study, but generally, soy and soy isoflavones are recognized for their health benefits, including their benefit for cardiovascular disease risk.

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