Recently, 12 healthy male volunteers ate a breakfast cereal containing 18% inulin for several weeks. At the end of the trial, plasma total cholesterol and triacylglycerol levels were significantly decreased.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Inulins are contraindicated in those who are hypersensitive to these substances.

PRECAUTIONS

Those who develop gastrointestinal symptoms with the use of dietary fiber should exercise caution in the use of inulins. Those with irritable bowel syndrome should exercise caution in the use of inulins. Those receiving whole body-radiation or radiation to the gastrointestinal tract should avoid supplementation with inulins.

ADVERSE REACTIONS

Doses up to 10 grams daily are well tolerated. Higher doses may cause such gastrointestinal symptoms as flatulence, bloating and diarrhea.

Occasional allergic reactions have been reported.

INTERACTIONS

NUTRITIONAL SUPPLEMENTS

Inulins may enhance the colonic absorption of calcium and magnesium supplements if used concomitantly with them.

Probiotics: The possible beneficial effects of inulins may be enhanced if used in combination with probiotics.

FOODS

Inulins may enhance the colonic absorption of calcium and magnesium in foods.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

Inulins are available in tablets, powder and functional foods. Dosing is variable and ranges from 4 to 10 grams daily. Those who use more than 10 grams daily should split the dosage throughout the day. Doses higher than 30 grams daily may cause significant gastrointestinal discomfort.

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Iodine

DESCRIPTION

Iodine, consumed principally as its iodide salts, is an essential trace element which is vital to the function of the thyroid gland. It is an essential component of thyroid hormones, which are required for normal development and metabolism. The fact that trace element composition of foods is very much dependent on geography was first recognized with respect to iodine. Iodine is present in low amounts in the earth's crust and thus in its soil. It is plentiful in the oceans and is found in sea animals and sea plants, such as seaweeds. Iodine is a non-metallic element belonging to the halogen group. Its atomic number is 53, and its atomic mass is 126.90 daltons. Its atomic symbol is I. The terms iodine and iodide are frequently used interchangeably.

The thyroid hormones are iodine-containing substances and they do not function without iodine. Approximately 80% of the body's iodine pool, or about 15 milligrams in adults, is present in the thyroid gland. Moderate deficiency of iodine may result in a goiter. Severe iodine deficiency may result in endemic myxedema among adults and in endemic cretinism among infants. Iodine deficiency results in decreased production of the thyroid hormones thyroxine or T_4 and triiodothyronine or T_3. The fall in the level of T_4 leads to increased thyroid stimulating hormone (TSH) output from the pituitary gland, resulting in an increase in the size of the thyroid gland which can lead to the formation of a goiter. In addition to causing goiters, iodine deficiency may result in a wide spectrum of effects on growth and development, particularly on brain development. Iodine deficiency is the most common cause of preventable mental deficit in the world.

In the early 1900s and prior to that, iodine deficiency and endemic goiter were very common in the United States. In the early 1920s, it was demonstrated in school children in Ohio that endemic goiter could be prevented and reduced by administration of small amounts of iodine in the form of iodide. Shortly afterwards, mass prophylaxis of endemic goiter with iodized salt was introduced in the United States and Switzerland, leading to a sharp fall in the incidence of goiter, as well as cretinism. Goiter, myxedema and other

iodine deficiency disorders (IDD), including cretinism, still continue to be major public health problems on the global level. Approximately 20% of the world's population is iodine-deficient and at risk for IDD.

In addition to iodized salt, rich sources of iodine include fish and sea vegetables (seaweeds). Iodine is also available in animal products, such as eggs, milk, meat and poultry. In industrialized countries, most animal feeds are enriched with iodine.

ACTIONS AND PHARMACOLOGY

ACTIONS

Iodine's major action is its precursor role in the formation of thyroid hormones. Iodine may also be protective against radioactive iodine and consequent thyroid cancer. Iodine is used therapeutically for the treatment of certain hyperthyroid conditions and thyroid storm. The radionuclide ^{123}I is used for thyroid imaging and ^{131}I is used therapeutically for radioactive ablation of benign overactive thyroid and of locally invasive or metastatic thyroid cancer.

MECHANISM OF ACTION

Iodine in the form of iodide is preferentially taken up by the thyroid gland. Iodide is accumulated in the thyroid by means of an active iodide transport mechanism which is catalyzed by a sodium/iodide symporter, which mediates the sodium/potassium ATPase-dependent coupling of inward iodide and sodium fluxes. The thyroid gland is not the only organ capable of iodide uptake. However, the thyroid is the only organ known to organify iodide. Iodide is released by the thyroid cells into the colloid follicle phase, and there it is oxidized by hydrogen peroxide formed from the thyroid peroxidase system. Iodine reacts with tyrosine residues in thyroglobulin to form thyroxine (T_4 and triiodothyronine (T_3. The formation of T_4 and T_3 takes place post-translationally. The iodinated thyroglobulin is absorbed back into the thyroid cells where proteolytic enzymes break it down. The thyroid hormones T_4 and T_3 are released into the circulation and distributed to the various tissues of the body.

Potassium iodide may be used following radiation exposure from a nuclear reactor accident. Pharmacological doses of iodide block uptake by the thyroid of radioactive isotopes, particularly ^{131}I, thus minimizing the risk of radiation-induced thyroid cancer.

PHARMACOKINETICS

Iodine in the form of iodide is rapidly and efficiently absorbed from the small intestine following ingestion. A large fraction of absorbed iodine is taken up by the thyroid gland via the sodium/iodide symporter. In addition to the thyroid gland, active iodide occurs in the salivary glands, the gastric mucosa and in the lactating mammary gland. The nonlactating mammary gland does not accumulate iodide. Recently, it has been reported that accumulation of iodide via a sodium/iodide symporter appears to occur in human breast cancer tissue. The major route of excretion of excess iodine is by the kidneys.

INDICATIONS AND USAGE

Apart from its use in iodine-deficiency disorders and for certain hyperthyroid conditions and thyroid storm, iodine is used as an expectorant and has demonstrated some ability to protect against the toxic effects of radioactive materials. It has also shown some preliminary efficacy in the treatment of sarcoidosis and has ameliorated some of the symptoms of fibrocystic disease of the breast. There are some preliminary reports that iodine is helpful in the treatment of erythematous dermatoses. Recently, some researchers have expressed concern that those on vegetarian diets may be at increased risk of iodine deficiency. Similarly, those on salt-restricted diets in general may be at the same or greater increased risk.

RESEARCH SUMMARY

There are reports that potassium iodide is a useful expectorant in chronic obstructive pulmonary disease including bronchitis, emphysema and asthma. It has been used in some studies of these conditions at doses of 300 to 1,000 milligrams two or three times daily. While somewhat effective, potassium iodide is not often used in this context due to the availability of more effective and safer expectorants.

Potassium iodide can effectively reduce thyroid uptake of radioiodine by 90% to 99% when administered immediately after exposure. Dosage used for this purpose has been reported at 130 milligrams per day. A 50% reduction in uptake of radioiodine has been achieved when potassium iodide was administered three to four hours after exposure to radiation. Limited benefit was seen when therapy began between four and twelve hours post-exposure. Potassium iodide has not protected against other radioactive substances.

The World Health Organization (WHO) has recommended that communities near nuclear reactors stockpile potassium iodides. Some credit Poland's prompt and widespread use of potassium iodide after the 1986 Chernobyl nuclear reactor disaster with the fact that Poland did not experience a significant increase in the incidence of childhood thyroid cancers, while fallout areas in Ukraine, Belarus and Russia (where potassium iodide was not widely used) have experienced large increases in these cancers.

Treatment with elemental iodine for four months has reportedly produced significant relief from symptoms of fibrocystic breast disease in one study. Upon discontinuing iodine, women in this study suffered a recurrence of pain and soreness. Some subsequent studies have also reported significant benefit from supplementation with other iodine-

containing compounds used to treat this condition. Sodium iodide exhibited marked efficacy but was accompanied by a high rate of side effects. In one analysis of three clinical studies, molecular iodine was found to be the most beneficial in the treatment of fibrocystic breast disease.

There is one case report in which 300 milligrams of potassium iodide three times daily was of significant benefit in subjects with sarcoidosis. Pain and swelling in the arthritic ankle largely disappeared within 48 hours after initiation of treatment, and there was rapid regression of erythema nodosum on the leg.

Some others have reported benefit from 200 milligrams of potassium iodide three times daily in subjects with erythema nodosum. Best response has been seen when given soon after onset in patients with positive C-reactive protein reactions. There is also very preliminary evidence that the same doses of potassium iodide may be helpful in some with erythema multiforme and nodular vasculitis. More research is needed to confirm these findings.

Recently, some researchers have concluded that vegetarians, especially "strict" vegetarians who exclude all animal products from their diets, may be at increased risk of iodine deficiency. Both strict vegan diets and lactovegetarian diets that exclude seaweed and iodized salt provide very low iodine, according to the findings of one recent study. Non-vegetarian diets that exclude iodized salt and naturally rich sources of iodine, especially fish and seafood, also deliver very little iodine.

Urinary excretion studies have suggested that there has been a decline in iodide intake in several populations tested, e.g., school children in Switzerland and blood donors in New Zealand. Some have attributed this to the growing popularity of salt-restriction in diet generally. Some European populations have also recently been reported to exhibit overt and borderline iodine deficiencies.

One researcher has concluded that "the subclinical effects of low iodine intake and the physiological significance of low iodine excretion need to be studied further."

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Iodide and iodine are contraindicated in those hypersensitive to iodide- and iodine-containing products.

PRECAUTIONS

Pregnant women and nursing mothers should avoid intakes of iodine (iodide) greater than RDA amounts. These amounts are 220 micrograms daily for pregnant women and 290 micrograms daily for nursing mothers. Use of iodide doses much higher than 220 micrograms daily by pregnant women may cause fetal damage. Use by nursing mothers of iodide doses much greater than 290 micrograms daily may cause rash and thyroid suppression in the infant.

Older people with nodular goiters are at risk of developing hyperthyroidism from use of potassium iodide and iodized salt.

Potassium iodide and iodized salt may exacerbate symptoms in some with autoimmune thyroiditis.

Children with cystic fibrosis appear to have an exaggerated susceptibility to the goitrogenic effect of high doses of iodide.

ADVERSE REACTIONS

Doses of iodide up to 1,000 micrograms daily are generally well tolerated. Pharmacological doses of iodide have caused a number of adverse reactions. The adverse reactions include hypersensitivity reactions, flare-up of adolescent acne, rashes, arrhythmias, central nervous system effects (confusion, numbness, tingling, weakness in the hands or feet), hypothyroidism, hyperthyroidism (Jod-Basedow phenomenon), parotitis (iodide mumps), thyroid adenoma and small bowel lesions.

Manifestations of hypersensitivity reactions include angioedema, symptoms resembling serum sickness (fever, arthralgia, eosinophilia, lymphadenopathy), cutaneous and mucosal hemorrhages, urticaria, thrombotic thrombocytopenia purpura (TTP) and fatal periarteritis. Nonspecific small bowel lesions manifested by stenosis with or without ulcerations have been associated with the use of enteric-coated potassium iodide. These lesions may cause hemorrhage, obstruction, perforation and death.

Chronic intake of pharmacological doses of iodides can lead to iodism. Iodism is characterized by frontal headache, pulmonary edema, coryza, eye irritation, skin eruptions, gastric disturbances and inflammation of the tonsils, larynx, pharynx and submaxillary and parotid glands.

The most common adverse effect of salt iodization is the development of iodine-induced hyperthyroidism (IIH). IIH affects mainly older people with nodular goiter. Another possibility is the exacerbation of autoimmune thyroiditis. Theoretically, salt iodization can induce hypothyroidism by acute blockage of the synthesis and secretion of thyroid hormones. Hypothyroidism, however, has not been reported with salt iodization. Also, allergic responses to salt iodization are rare. IIH may develop when iodine deficiency increases thyrocyte proliferation and mutation rates. This can lead to the development of hyperfunctioning autonomous nodules in the thyroid gland and hyperthyroidism following iodine supplementation. A recent study reported transient hyperthyroidism in one out of 32 young adults with goiter

and hypothyroidism after receiving 200 micrograms daily of iodine.

INTERACTIONS

DRUGS

Antithyroid Drugs: Concomitant use of antithyroid drugs and iodide may potentiate the hypothyroid effect of iodides.

Lithium: Concomitant use of pharmacological doses of potassium iodide and lithium may result in hypothyroidism.

Warfarin: Concomitant use of pharmacological doses of potassium iodide (for hyperthyroidism) and warfarin may decrease the anticoagulant effectiveness of warfarin.

NUTRITIONAL SUPPLEMENTS

Selenium: Intake of selenium and iodide may have synergistic activity in the treatment of Kashin-Beck disease, an osteoarthropathy (see Selenium).

FOODS

Certain foods contain substances which are metabolized to 5-vinyloxazolidine-2-thione and thiocyanate. 5-Vinyloxazolidine-2-thione and thiocyanate may compete with iodide and negatively affect the iodine status of the thyroid gland and may cause hypothyroidism. These food substances are called goitrogens and are found in foods such as cassava and such cruciferous foods as cabbage, Brussels sprouts, broccoli, cauliflower and rutabaga. Certain flavonoids may have goitrogenic activity. C-gluosylflavones such as vitexin, which are found in millet, have been found to inhibit thyroid peroxidase activity. The soybean isoflavones genistein and daidzein have also been found to inhibit thyroid peroxidase.

OVERDOSAGE

The administration of pharmacological doses of potassium iodide to those with impaired renal function may lead to serious hyperkalemia.

DOSAGE AND ADMINISTRATION

Potassium iodide is available as a nutritional supplement, typically in combination products. Doses are usually 150 micrograms daily for adults.

Approximately 77% of potassium iodide is comprised of iodide.

Iodine is commonly available in iodized salt. Iodine content in iodized salt ranges from 20 to 40 milligrams per kilogram or 20 to 40 micrograms per gram. Kosher salt typically does not contain iodine. Chefs in many of the better restaurants prefer using kosher salt to iodized salt.

Iodized oil is used in some countries as a dietary iodine source.

The median intake of iodine from food in the United States is approximately 240 to 300 micrograms/day for men and 190 to 210 micrograms/day for women.

Dietary Reference Intakes (DRI) for iodine by age group (micrograms/day) are as follows:

Infants	Adequate Intake (AI)
0-6 months	110
7-12 months	130
Children	**Recommended Daily Allowance (RDA)**
1-3 years	90
4-8 years	90
Boys	
9-13 years	120
14-18 years	150
Girls	
9-13 years	120
14-18 years	150
Men	
19-30 years	150
31-50 years	150
51-70 years	150
Older than 70 years	150
Women	
19-30 years	150
31-50 years	150
51-70 years	150
Older than 70 years	150
Pregnancy	
14-18 years	220
19-30 years	220
31-50 years	220
Lactation	
14-18 years	290
19-30 years	290
31-50 years	290

The following summarizes the Tolerable Upper Intake Level (UL) for various age groups and conditions:

Infants	
0-6 months	ND
7-12 months	ND
Children	
1-3 years	200
4-8 years	300
9-13 years	600

Adolescents	
14-18 years	900
Adults	
19 years and older	1,100
Pregnancy	
14-18 years	900
19 years and older	1,100
Lactation	
14-18 years	900
19 years and older	1,100

UL = Tolerable Upper Intake Level
ND = Not Determinable

The DV (Daily Value) for iodine, which is used for determining percentage of nutrient daily values on nutritional supplement and food labels, is 150 micrograms. The basis for the DV for iodine is the 1973 U.S. RDA.

The World Health Organization's (WHO) recommendations are slightly different and are:

Age (years) or status	Intake (micrograms/day)
0 to 1	50
1 to 6	90
7 to 12	120
Greater than 12	150
Pregnancy	200
Lactation	200

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Ipriflavone

DESCRIPTION

Ipriflavone is a synthetic derivative of the plant isoflavone, genistein. Genistein is mainly found in soya in the form of genistin but also found in other plant sources, as well, in lower amounts. Ipriflavone occurs in trace amounts in some soy sauces. Although ipriflavone is sometimes classified as a phytoestrogen, it has no direct estrogenic activity. Ipriflavone does not activate any of the estrogen receptors. It does appear to have a favorable impact on bone density, and ipriflavone has been approved for the treatment of involutional osteoporosis in some European countries and in Japan.

The structural formula of ipriflavone is: