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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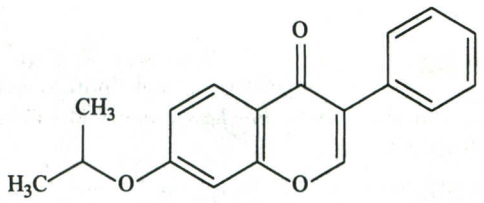
Ipriflavone

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:



Ipriflavone

Ipriflavone is also known as 7-isopropoxy-3-phenyl-4H-1-benzopyran-4-one; 7-(1-methylethoxy)-3-phenyl-4H-1-benzopyran-4-one; 7-isopropoxy-3-phenylchromone and 7-isopropoxyisoflavone. Ipriflavone is abbreviated as IP. It is a solid substance that has poor solubility in water.

ACTIONS AND PHARMACOLOGY

ACTIONS

Ipriflavone may have a beneficial action on bone density.

MECHANISM OF ACTION

Osteoporosis is the consequence of an imbalance between osteoclastic and osteoblastic activity, coupled with an increased rate of bone turnover that occurs with menopause. Osteoclasts are the bone-resorbing cells, and osteoblasts are the bone-forming cells. In osteoporosis, a net loss of bone mass occurs due to either excessive-bone-resorbing activity of osteoclasts or impaired bone-forming activity of osteoblasts.

In vitro and animal studies suggest ipriflavone inhibits osteoclastic bone resorption and that it may also stimulate bone formation. Ipriflavone does not possess any estrogenic activity. The mechanism of action of ipriflavone on osteocasts and their precursor cells is not well understood. There is some evidence that ipriflavone may stimulate osteoblast activity by down-regulation of endothelin receptors. Ipriflavone may also reduce the ability of endothelin-1 to inhibit mineralization. Ipriflavone was found to be effective in preventing bone loss in ovariectomized rats. Ipriflavone, in contrast to estradiol, did not lower ovariectomized-induced rise in serum alkaline phosphatase or insulin-like growth factor-1 (IGF-1) and IGF-1 binding protein (IGFBP-3) concentrations.

PHARMACOKINETICS

Ipriflavone is absorbed from the small intestine; from there it enters the portal circulation. Greater absorption is obtained with food, and lipid-containing foods especially enhance its absorption. Ipriflavone is metabolized in the liver. The two major metabolites are 7-hydroxy-ipriflavone and 7-(1-carboxy-ethoxy)-isoflavone. Ipriflavone and its metabolites are distributed to the various tissues of the body via the systemic circulation.

In the blood, ipriflavone and its metabolites are bound to albumin. Elimination of ipriflavone and its metabolites is mainly by the urinary route. A smaller fraction of ingested ipriflavone is eliminated in the feces.

INDICATIONS AND USAGE

Ipriflavone may be indicated to help prevent and reduce bone resorption in osteoporosis. It may also help relieve bone pain associated with osteoporosis. There is some evidence that it can help correct some lipid disturbances associated with estrogen deficiency. Because ipriflavone does not have direct estrogenic effects, it may be suitable for use in aging men with bone loss, as well as in women. It has been suggested that ipriflavone might help prevent or reduce bone loss in men who have prostate cancer and are receiving androgen-reducing therapies.

RESEARCH SUMMARY

Ipriflavone is a currently approved drug indicated for the treatment and prevention of osteoporosis in Japan, Italy, Hungary and some other countries. It is available as a supplement in the United States. Its efficacy is increased when it is combined with calcium and other supplements that help diminish bone loss associated with menopause and aging. It is also sometimes combined with low-dose estrogen preparations.

Ipriflavone's efficacy in osteoporosis is well established by the results of numerous clinical studies, as well as studies involving many animal models. Many carefully controlled studies demonstrate that oral doses of 200 milligrams of ipriflavone three times a day (often combined with one gram of oral calcium daily) can have significant effects, increasing bone mineral density, reducing bone pain and diminishing the incidence of bone fractures—usually in post-menopausal women. Significant improvements in mobility have also been observed. Some studies have continued for as long as two years without incidence of significant side-effects.

Ipriflavone may exert its beneficial effects by inhibiting formation of the osteoclasts that are involved in bone resorption and by promoting the activity of the osteoblasts involved in building new bone. Its lack of direct estrogenic effects may make it a useful alternative in some cases to standard therapies and may, in particular, make it a useful therapy in men with bone loss associated with aging or androgen-limiting therapies (such as those sometimes used in the treatment of prostate cancer). More study is needed to determine ipriflavone's efficacy in this context.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to an ipriflavone-containing product.

PRECAUTIONS

Because of lack of long-term safety studies, ipriflavone should be avoided by pregnant women and nursing mothers. Those taking theophylline should be aware of an interaction with ipriflavone causing higher theophylline levels.

ADVERSE REACTIONS

Mild gastrointestinal side effects such as nausea have been reported.

INTERACTIONS

DRUGS

Theophylline: Ipriflavone is reported to inhibit the metabolism and elimination of theophylline. Both ipriflavone and its metabolite 7-hydroxy-isoflavone inhibit CYP (cytochrome P450) 1A2 and also CYP2C9. Inhibition of cytochrome P450 metabolism of theophylline produces higher serum levels of theophylline per given theophylline dose and, therefore, those on theophylline who also take ipriflavone must have their serum theophylline levels carefully monitored in order to avoid any toxic effects of elevated theophylline levels.

Tolbutamide: Ipriflavone and 7-hydroxy-ipriflavone inhibit tolbutamide hydroxylase activity. Consequently, use of ipriflavone may be expected to give higher levels of tolbutamide when the two are administered concurrently.

Nifedipine: 7-hydroxy-ipriflavone inhibits nifedipine oxidase activity. Consequently, use of ipriflavone may be expected to give higher levels of nifedipine in those using these products together.

Estrogen: Ipriflavone may add to the effects of estrogen.

SERM's: Ipriflavone may add to the effects of selective estrogen receptor modulators (SERMs).

Calcitonin: Ipriflavone may add to the effects of calcitonin.

Biophosphonates: Ipriflavone may add to the effects of and biophosphonates in the management of osteoporosis.

NUTRITIONAL SUPPLEMENTS

Ipriflavone may add to the effects of vitamins D and K, calcium, fluoride and boron in the management of osteoporosis.

OVERDOSAGE

There are no reports of ipriflavone overdosage.

DOSAGE AND ADMINISTRATION

The typical dose for use in the management of osteoporosis is 200 milligrams taken twice or three times daily.

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Iron

DESCRIPTION

Iron is an essential trace mineral in human nutrition. It is involved in the entire process of respiration, including oxygen transport and electron transport. The principal goal of respiration is the production of biologic energy. Iron-deficiency, which can lead to a microcytic, hypochromic anemia, is the most common nutritional disorder in the world. Approximately 25% of the world's population is iron-deficient. Even iron-deficiency states which do not lead to anemia may have global effects on human health. On the other hand, iron overload disorders, which can lead to