

HUMET (Humifulvate)

The FDA has approved Humifulvate (Humet) for introduction into the USA as a dietary supplement. Extracts from the detailed scientific information provided to the FDA is listed below. Used in Europe to treat a wide range of health problems related to Heavy metal toxicity, Cardiovascular Disease (plaque removal), certain cancers, Psoriasis, Eczema, anemia, the immune system and general well being, the potential exists to apply to the FDA for approval of Humet as a drug for the treatment of several serious diseases.

The significance of Humifulvate: Toxic metal poisoning is associated with many diseases and health problems. Once in a lifetime, a natural product of this significance enters the market. Researched and developed over many years in Hungary, HUMET is now available in the United States through Life-flo Health Care Products and Allvia Integrative Pharmaceuticals in Phoenix. AZ.

Toxic Metal Poisoning: The sources by which such metals enter the body include: Drinking Water, Air Pollution, Tobacco, Fish and Seafood, Antiperspirants, Pesticides, Fertilizers, Medications, Aluminum Cookware, Amalgam Fillings, Heavy Traffic and Old Paint.

Chelation Therapy: Chelating has mostly been associated with the chemical EDTA, but Chelation refers to any agent that removes toxic contaminants (heavy metal poisoning) from the body.

Humifulvate an oral chelate: Humifulvate is a highly efficient oral Chelate that attaches to the toxic heavy metals – Mercury, Cadmium, Lead, Arsenic, Copper, Thallium and Aluminum and discharges them from the body. **Humifulvate** is 10 times more effective than oral EDTA.

Cancer, cardiovascular disease (plaque removal) and general well being are amongst the most common health problems treated by EDTA, especially by the, complimentary , and alternative medicine doctors. Many other diseases are also associated with heavy metal poisoning. For many years, EDTA has been the standard method used by the medical profession, (and more recently by alternative or complimentary doctors) to remove toxic metals and treat diseases associated with heavy metal poisoning. ACAM (American Academy of Alternative Medicine) has been a major proponent of Chelation Therapy using EDTA.

Diseases and Health Problems Associated with Heavy Metal Poisoning

Cardiovascular problems

Blood vessel damage, hypertension, decreased red blood cell count, peripheral vascular disease, cardiovascular disease, vascular collapse.

Renal and Hepatic impairment

Cancers (particularly colon, pancreatic, stomach and rectal), Liver and kidney impairment

Respiratory system Issues

Respiratory tract cancers, asthmatic conditions, pneumonia, pulmonary edema, pulmonary fibrosis

Reproductive problems

Genital abnormalities, menstrual pain, birth defects Immune system deficiencies, Immunosuppression, inhibition of lymphocytes, T-cells, monocytes, decreased white blood cell count.

Hair loss

Alopecia

Skin disorders

Rashes, dermatitis, eczema, irritated skin.

Cognitive impairment

Dementia and impaired reaction time etc, mental impairment, poor memory, difficulty understanding abstract ideas or carrying out complex commands.

Nervous system

Loss of feeling and numbness in the extremities

Physiological impairment

Nerve conductivity, spinal cord, abnormal EEG's etc.

Motor disorders

Difficulty walking, talking and swallowing, myoclonal jerks, loss of balance, problems sitting or lying and seizure etc.

Sensory: abnormalities

Abnormal sensations in the mouth and extremities, hearing loss, diminished touch sensations, blurred vision and sensitivity to light).

Physical disturbances

Decreased muscular strength, headaches, and colic.

Speech problems

Such as comprehension deficit, slurred speech, loss of speech or development problems with language, speech comprehension deficit, articulation problems, slurred speech, unintelligible speech.

Psychiatric disturbances

Social withdrawal, stereotyped behavior, depression and mood swings, schizoid tendencies, aggressive behavior, suicidal behavior, sleep difficulties, chronic fatigue, Weakness, malaise, eating disorders, anxiety and nervous tendencies, ADHD, eye contact problems, impaired visual fixation.

What is Humet?

Humet is a colloidal mix of humifulvate and ten organic minerals: Iron, Magnesium, Zinc, Copper, Cobalt, Manganese, Selenium, Vanadium, Molybdenum and Potassium, which is released into the body and the freed humic acids then naturally bond to any heavy metal molecules (cadmium, mercury, lead, etc) and these are removed in the waste.

This colloidal mix forms an optimal carrying agent with the humic acids providing, valuable function groups which contain trace elements and minerals in chelated biochemical structures similar to the human body's own transport-proteins. These are easily absorbed and have high bioavailability. Humet carry's the international Recommended Daily Allowances (RDA) of the ten organic minerals.

Humifulvate is derived from Hungarian peat found primarily along the northern shores of Lake Balaton in Hungary. The raw material is processed in clean room conditions under the strict supervision of the Hungarian FDA into a concentrate for conversion to liquid and solid forms for oral consumption. In the USA, Humet has been classified as a dietary supplement.

Humifulvate is a distinct and identifiable mixture of humic, fulvic and phenolic acids in a humate/polyphenolic complex. A torpha torf prepararate (TTP) byproduct of the incomplete natural decomposition (humification) of organic plant material with origins of 3000 to 10,000 years.

No negative side effects

Humet possesses none of the dangerous or negative side effects of EDTA

EDTA side effects: Side effects from the chemical EDTA include dangerously low calcium blood levels, decrease of ability to make new blood cells - damage to bone marrow, kidney damage (with elevated creatinine levels) very low blood pressure, fast heart rate, increased risk of bleeding or blood clots (including interference with the effects of blood thinning drug warfarin (Coumadin) bacterial blood infections, seizures, allergic or immune system reactions, hearty rhythm abnormalities and unstable blood

sugar. Other side effects may include fever, nausea, vomiting, gas, intestinal upset, excessive thirst, sweating (diaphoresis) headache, decreased thyroid function, fatigue, low white blood cell count (leukopenia), or low blood platelet count (thrombocytopenia). Severe reactions have occurred in which people have stopped breathing. EDTA may be dangerous in individuals with heart, kidney, or liver disease or with conditions affecting blood cells or the immune system. Use during pregnancy, breastfeeding or in children may also be dangerous due to potential toxic effects.

EDTA a heavy metal chelating agent was first synthesized in the early 1930's and in the 1950's this chemical became widely used to treat heavy metal poisoning, and in particular, lead poisoning. Some observers noted that benefits occurred in patients with diabetes and clogged arteries in the heart or legs as well as benefits for many other conditions.

It has been proposed that EDTA may be beneficial for other conditions including breaking down cholesterol plaques in the arteries. Other mechanisms such as removal of calcium from these plaques and antioxidant properties have also been suggested.

Today many "alternative doctors tout the benefits of EDTA Chelation Therapy and about 2000 doctors in the USA are known to offer chelation therapy as a significant part of their practice for the treatment of heart disease and cancer as well as for general well being. However, the use of EDTA as a treatment for clogged arteries or peripheral vascular disease is not scientifically supported and research is ongoing in this area.

Marketing in the USA

In the USA Humifulvate and Humet is marketed as a dietary supplement for increasing overall Vitality and promoting overall health.

Humifulvate is the active Chelating ingredient derived from a very unique Peat found along the Northern shores of Lake Balaton in Hungary. Humet is the name of the products which have been formulated with Humifulvate as the main active ingredient. Humet is a colloidal mix of humifulvate at the recommended dosage plus ten organic minerals: Iron, Magnesium, Zinc, Copper, Cobalt, Manganese, Selenium, Vanadium, Molybdenum and Potassium formulated to provide the RDA for these organic minerals.

Extracts from the Medical, scientific and research data provided on Humifulvate to the FDA

Extensive scientific research ~ established that this (Hungarian) peat deposit is slightly alkaline (pH 7-8), has an ash content of 28% to 43%, and contains significant quantities of two predominate humate compounds, humic acid and fulvic acid, along with minor amount of phenolic acid. The peat deposit also contains calcium huminate, a degradation product of lignans, shell remnants, calcareous materials and other minerals.

Humic and fulvic acids are multi-substituted polyaromatic heterocyclic macromolecules that incorporate protocatechic acid, vanillic acid, vanillin, resorcinol, ferulic acid, benzoic acid and other cyclic polyphenols resulting from the degradation of the structural lignans in plant cells walls. These constituents of humic and fulvic acids are rich in carboxyl, hydroxyl, and carbonyl groups as well as in phenols, quinones and semiquinones. [2-4] Within each macromolecule, aromatic groups are linked by amino acids, amino sugars, peptides and other aliphatic carbon chains similar to those found within the human body. Fulvic acids obtained from peat may represent degradation products of humic acids, contain more oxygen-rich reactive groups than do humic acids, and are of smaller molecular weights than are humic acids.

Despite the complexity in its composition, infrared spectroscopic analyses have revealed that Humiffulvate is a distinct mixture of predominantly humic and fulvic acids; therefore, the humate/polyphenolic complex is referred to by the term, Humiffulvate.

Humiffulvate is a negatively charged metal complexing ligand. There are a number of active sites where metal ions may bind to aromatic and aliphatic carboxyl and phenolic hydroxyl groups within the Humiffulvate complex, allowing Humiffulvate to act as an ion exchanger, releasing metal ions of low atomic mass and chelating heavier metals. These properties are abolished by either methylation or acetylation of the reactive sites.

Humiffulvate concentrate (HFC) consists of Humiffulvate in combination with minerals and trace elements. Research results suggest that HFC enhances mineral and trace element status, supporting the maintenance of mineral and trace element balances without bypassing normal homeostatic mechanisms for preventing mineral toxicity. Following dissociation of the minerals and trace elements delivered by HFC, the residual Humiffulvate complex may chelate heavy metals along the intestinal tract, thereby reducing heavy metal burdens.

Level of Humiffulvate in Dietary Supplements

Humiffulvate is supplied as a dietary supplement in combination with defined amounts of several minerals and trace elements.

A single daily dose (10 ml) of Humiffulvate {HFC) contains, in liquid or solid form:
Humiffulvate.....75 mg (47.86%)

The Conditions of Use Recommended in Labeling of Ordinary Course of Use of Humifulvate (Structure/Function Claims with references

Humifulvate concentrate (HFC) supports normal mineral and trace element homeostasis.

Two weeks of oral administration of HFC (313.4 mg/day, providing 150 mg of Humifulvate daily) was associated with increased blood copper concentrations and improved iron metabolism in 51 healthy adult volunteers. [14] In another uncontrolled study, oral consumption of HFC (156.7 mg/day) for 6 weeks resulted in significant increases in initially low serum iron concentrations. [15] Similarly, serum iron concentrations improved in 14 healthy adults consuming HFC for 3 weeks (156.7 mg/day); in all subjects with initially depressed serum iron or ferritin concentrations, those concentrations approached the respective normal physiologic ranges within the 3 weeks of treatment. [16] In addition, those subjects with supranormal prestudy serum iron concentrations exhibited decreases in serum iron concentrations during the study. In 19 pediatric patients with iron deficiency anemia, serum iron concentrations began to increase within 2 weeks of oral treatment with HFC (31.4 mg BFC/10kg body weight/day) and were significantly increased after 3 weeks of therapy.[17]

In an investigation of the bioavailability of the trace minerals provided adult rats that had been fed a diet deficient in trace minerals for 2 weeks were supplemented with either HFC, at daily dose equivalent to the recommended human daily dose, or an inorganic mixture of salts, identical in composition and daily dosage to the trace minerals in HFC. [18] Following 2 weeks of replacement feeding, whole-body retentions of oral doses of radio labeled cobalt, iron, zinc, selenium and copper were the same regardless of the form of trace minerals. In addition, the intestinal absorption of dietary iron was significantly increased by HFC.

The benefits of HFC supplementation on mineral and trace element homeostasis appears to be unmistakable to newborn progeny: In one experiment, piglets born to iron deficient sows that had been supplemented with HFC (1500 mg daily, providing 7 17.9 mg of Humifulvate) during gestation exhibited significantly higher plasma hemoglobin concentrations than did piglets born to iron deficient sows that had received standard parenteral iron supplementation or no treatment.[19] Similarly, the pups of Sprague-Dawley rats that had been fed iron deficient diets plus HFC (10 mg/kg daily, providing 4.8 mg/kg of Humifulvate) exhibited plasma hemoglobin concentrations, hematocrits, and transferrin saturation similar to those of pups born to iron deficient dams that had received supplemental iron.[20] Newborn pups of rats fed a trace mineral deficient diet supplemented throughout gestation with IIFC at a daily dose equivalent to the recommended human daily dose had significantly greater whole-body contents of cobalt and zinc than did newborn pups of rats fed the same trace mineral deficient diet supplemented with equivalent amounts of inorganic trace mineral salts.[18]

Humifulvate concentrate (HFC) supports normal physiologic utilization of minerals and trace elements.

Improvements in appetite and general well being in pediatric patients with iron deficiency anemia were attributed to treatment with HFC for 3 weeks (3 1.4 mg HFC/10kg body weight/day).[17] Daily oral administration of HFC (4.5 mg/kg body weight, providing 2.2 mg/kg of Humifulvate) to nine children with chronic eczema resulted in marked improvement in the degree of eczema in eight of the children in 3 weeks.[17] Cyclic discontinuation and reinstatement of supplementation were associated with exacerbation and amelioration, respectively, of disease severity.

Among a set of case reports [21-24] describing the effectiveness of HFC (156.7 mg/day, providing 75 mg Humifulvate daily, for varying lengths of time) as an adjuvant during gyrostatic therapy in patients with confirmed tumors, one group of patients was reported to exhibit enhanced erythropoiesis during supplementation[24] and all groups of patients reported improvements in appetite, weight gain, general resistance to stress and capacity to work, while nausea, fatigue and need for analgesics were reduced. In a group of 29 adults experiencing hair loss attributed to trace element deficiencies who were treated with HFC (156.7 to 313.4 mg/day, providing 75 to 150 mg Humifulvate daily, for 4 to 6 weeks), subjects who exhibited increases in serum iron concentrations also exhibited improvements in hair growth and regeneration. [25] Among a select group of 25 elite adult athletes who added HFC to their training regimens for 3 weeks (313.4 mg/day), most of the subjects reported perceptions of increased resistance to the stress of training and enhanced ability to

Focus During Training Bouts.[26]

Rats fed HFC (10 mg/kg, providing 4.8 mg/kg of Humifulvate) daily for 14 days prior to ischemic insult experienced greater coronary blood flow, aortic blood flow and left ventricular end diastolic pressure following insult than did placebo-fed rats, suggesting that HFC may be cardioprotective.[27] Female adult rats given HFC (960 mg/kg, providing 459.5 mg/kg of Humifulvate) prior to whole body irradiation exhibited significantly faster recovery of platelet counts following irradiation.[28]

Humifulvate concentrate (HFC) supports the healthy reduction of heavy metal burdens.

Humifulvate concentrate (I-BC) contains negatively charged functional groups that contribute to the elimination of heavy metals stored in cells by organic bonding that resembles the transport of metalloproteins. Oral HFC has been demonstrated to increase urinary excretion of cadmium [15] and to decrease blood concentrations of cadmium [14,15,29] and lead [14,29-32] in adults treated with 156.7 to 313.4 mg/day (providing 75 to 150 mg/day of Humifulvate) for 3 to 12 weeks. Oral HFC also has been reported to inhibit the intestinal absorption of cadmium and lead from food as well: as their uptake from environmental sources.[14]

When radiolabeled strontium bound to Humiffulvate was fed to adult rats, the intestinal absorption and subsequent incorporation into bone of radio labeled strontium was lower than when similar rats were fed free radioactive strontium salt.[33] In adult pigs fed 31.3" to 313.4 mg HFC daily (pr~) Viding 15 to 150 mg/day of Humiffulvate), urinary excretion of mercury was significantly increased.[34] Isolated humic acid has inhibited the absorption of cadmium by rat intestine [35] and has reduced the accumulation of cadmium in the kidneys of rats. [36] Following 2 weeks of a trace mineral deficient diet, adult rats given oral IIFC (at a dose equivalent to the recommended human daily dose) for 2 weeks exhibited significantly more rapid excreti0!! of an oral cadmium burden, compared to similar rats given replacement trace minerals as inorganic salts.[18]

History of Use and Evidence of Safety

History of Use of Humiffulvate

The Humiffulvate found in HFC has been reviewed and approved by the Hungarian National Institute of Pharmacy. Humet -R syrup is registered in Hungary as a non-prescription preparation (GYI-430/1993).

Typical cumulative exposure to Humiffulvate during historical use can be estimated. Use of Humiffulvate, HFC , as recommended (150. / mg/day of the supplement, containing 75 mg/day of Humiffulvate, Humiffulvate, for up to 2 months), results in the cumulative consumption of up to 9402 mg of Humiffulvate concentrate, of which 4500 mg will be Humiffulvate, Humiffulvate. In addition, use of Humiffulvate as recommended results in typical cumulative exposure of up to 2202 mg of elemental potassium, 900 mg of elemental magnesium, 840 mg of elemental iron, 600 mg of elemental zinc, 180 mg of elemental manganese, 120 mg of elemental copper, 30 mg of elemental vanadium, 12 mg of elemental cobalt, 10.5 mg of elemental molybdenum and 7.5 mg of elemental, selenium.

Evidence of Safety of Humiffulvate

Toxicological and mutagenicity studies evaluating the safety of Humiffulvate (Humiffulvate concentrate; HFC) containing Humiffulvate (Humiffulvate) provide data attesting to the safety of Humiffulvate. All toxicological studies, mutagenicity studies and studies on laboratory animals have utilized Humiffulvate, HFC. Independent laboratory analyses utilizing infrared spectroscopy and fingerprinting have confirmed the consistent composition of the standardized HFC used in these studies.

Documentation of the safety of the amounts of each mineral and trace element in HFC can be found in reference 12

Toxicology Studies

No signs of toxicity, gross organ pathology or death have been reported in single dose toxicity tests in male and female adult rats given up to 10,000 mg of standardized HFC . per kg body weight (equivalent to up to 4786 mg/kg of Humifulvate and about 80 times the typical cumulative human exposure to Humifulvate when HFC is used as recommended). Acute studies in rats and mice have revealed no toxicity in daily doses exceeding 1000 mg HFC per kg body weight (equivalent to 478.6 mg/kg of Humifulvate and about 500 times the typical daily human exposure to Humifulvate). The acute oral ID50 for HFC was determined by the National Institute of Food and Nutrition Science (OETI) in Budapest, Hungary, to be greater than 10,000 mg of HFC per kg body weight (about 80 times the typical cumulative human exposure to Humifulvate when HFC is used as recommended).[38] An independent testing laboratory(Pharmaceutical Control and Developing Laboratory Co., Ltd., Budapest, Hungary) determined HFC to be "practically nontoxic." [39]

During a "limit test," adult male and female rats given 600 mg/kg of HFC (providing 287.3 mg/kg of Humifulvate) within 24 hours exhibited no signs of weight loss or macroscopic organ pathology.[39] Isolated cases of pulmonary hemorrhage and emphysema., thymic hemorrhage, splenic hyperemia and uterine changes occurred with similar frequency in bath treated and matched control rats; it was reported that these findings were consistent with indications of agonal death. No other symptoms of toxicity or lethality were observed during 14 days of post-treatment observation. From these data it was determined that the maximal tolerable dose (MTD) of HFC is greater than 600 mg/kg within a 24-hour period (containing about 300 times the recommended daily dose of Humifulvate, if a dose of 150 mg of HFC is ingested by a 75-kg human).

Adult rats given a single dose of 960 mg/kg of HFC (providing 459.5 mg/kg of Humifulvate, about 8 times the typical cumulative human exposure to Humifulvate) exhibited no adverse reactions or signs of toxicity following sublethal whole body irradiation. [40]

Reports summarizing acute oral toxicity studies in laboratory animals are provided in references 41-43.

In controlled cumulative toxicity testing, adult rats were fed HFC at the LD50 (10,000 mg/kg) daily for 24 days; body weights, hematological variables indices of thyroid function and microscopic organ histology were unaffected by the supplement. [46] However, some treated rats exhibited splenic hemosiderosis and both control and treated rats exhibited signs of peribronchial lymphocytic infiltration. In another study, adult rats fed HFC at 5,15 or 50 mg/kg 4aily for 28 days (amounting to about 1.25,3.75 and 12.5 times the typical cumulative human exposure to Humifulvate, respectively) exhibited no effects of HFC on body weights, clinical chemistry, hematological variables, enzyme functions, or organs weights.[47] however, 3 weeks of HFC at ISO or 500 mg/kg daily (providing 71.8 or 239.3 mg/kg of Humifulvate daily and amounting to about 28 and 93 times the' typical cumulative human exposure to Humifulvate, respectively) was

associated with decreases in body weights and in liver and kidney weights, which the authors attributed to undocumented reductions in appetite.

Adult rats fed a diet deficient in trace minerals and supplemented with either HFC at a daily dose equivalent to that recommended for humans or an equivalent amount of inorganic trace mineral salts exhibited no differences in average body weights, organ weights (liver, lung, kidney, brain, heart, spleen), changes in these weights, total litter weights, individual birth weights of progeny, daily urine volumes and daily fecal weights.[18] however, adult rats given humic acid at the equivalent of 280 times the recommended human daily dose retained approximately 20% to 30% less dietary iron, zinc and selenium than did the rats fed HFC.

Groups of adult rats fed potassium humate providing either 60 or 240 mg/day of humic acid for 2, 4, 6 or 8 weeks -exhibited growth rates, food consumption rates, physical agility, kidney and liver weights, white blood cell counts, red blood cell counts, thrombocyte counts, mean blood cell volumes, mean thrombocyte volumes, plasma hemoglobin concentrations, hematocrits, mean hemoglobin contents per red blood cell and mean red blood cell hemoglobin concentrations that were not -different from those of control-fed rats.[48] There were no adverse reactions, signs of toxicity or deaths during 8 weeks of exposure to the equivalent of up to what would be 80% to 3 times the typical cumulative human exposure to Humifulvate if HFC is 50% humic acid.

Reports summarizing the effects of prolonged oral intake of HFC in rats are provided in references 44 and 45

The available scientific evidence indicates that Humifulvate is not toxic or harmful when ingested by laboratory animals in amounts equivalent to between 0.8 and 500 times the typical cumulative human exposure.

Mutagenicity Studies

HFC has been found to exhibit no mutagenic activity under the Ames test criteria, using the *Sulmonetra typliimurium* reverse mutation assay. in tests conducted by the Toxicological Research Center, Ltd., Veszprem, Szabadsagpuszta, Hungary. [5 I] Additional studies conducted by the Medical Research Institute, Budapest, Hungary, using human peripheral blood lymphocytes, also have indicated that HFC is not mutagenic and does not increase the number or frequency of chromosome aberrations (clastogenesis) under test conditions,(44,45,52] Some data from these tests further suggest that HFC may be mildly anticlastogenic in vitro under certain conditions. Taken together, these findings attest to the nonmutagenic nature of HFC and its primary component, Humifulvate.

Studies of Safety in Humans

The safety of HFC has been demonstrated in 525 individuals: 157 otherwise healthy adults being treated for elevated blood lead or cadmium concentrations;[53-56] 18 adults[57,58] and 12 children[58] being treated for overt signs of lead poisoning; 114 adults and children with cancers;[59,60] 60 children with iron deficiency anemia, alopecia, eczema or severe illness;[61] and 164 healthy adult volunteers, including 36 elite athletes in training. [62-66]

The results of most of these studies of the safety of HFC in humans have been reviewed by the appropriate governmental agencies in Great Britain, Taiwan, Portugal, Russia, Lithuania, and the Netherlands prior to those agencies granting approval for the over-the-counter marketing of HFC as an oral dietary supplement in their respective countries. Additional details of these studies are compiled in reference 12.

The results of most of these studies of the safety of HFC in humans have been reviewed by the appropriate governmental agencies in Great Britain, Taiwan, Portugal, Russia, Lithuania, and the Netherlands prior to those agencies granting approval for the over-the-counter marketing of HFC as an oral dietary supplement in their respective countries. Additional details of these studies are compiled in reference 12.

No adverse events, subject complaints or laboratory evidence of adverse effects were noted in an open-label study of a single cohort of 30 otherwise healthy adults with elevated blood cadmium concentrations who were given HFC (156.7 mg/day, providing 75 mg of Humifulvate) daily for 6 weeks (equivalent to 75% of the typical cumulative human exposure).[53] Similarly, there was no difference in the occurrence of adverse reactions or events among 20 healthy adult subjects with elevated blood lead concentrations given HFC (313.4 mg/day, providing 150 mg of Humifulvate) or 15 similar subjects given placebo for 6 weeks in an open-label controlled trial (HFC consumption equivalent to 150% of the typical cumulative human exposure to Humifulvate).[55] In 2 open-label uncontrolled studies, another 207 healthy adults with elevated blood lead concentrations were reported to experience one case of gastrointestinal discomfort and one case of skin allergic reaction' during either 3 weeks of HFC treatment (147 subjects; 156.7mg/day; equivalent to 37.5% of the typical cumulative human exposure to Humifulvate)[54] or 12 weeks of HFC treatment (60 adults; 156.7 mg/day; equivalent to 150% of the typical cumulative human exposure to Humifulvate). [56]

Another 128 healthy adults who were given HFC (156.7 mg/day or 313.4 mg/day) daily for 2 to 6 weeks (with cumulative ingestion of HFC of up to 150% of the typical cumulative human exposure to Humifulvate) in 3 open label uncontrolled studies reported only 2 instances of "abdominal pressure and nausea" and one case of "softer feces." [62,63,65] In 2 open-label uncontrolled experiments on a total of 36 elite adult athletes, HFC at 313.4 mg/day for 3 to 4 weeks (equivalent to 75% to 100% of typical

cumulative human exposure) resulted in no reported adverse reactions or subject complaints. [64,66]

Taken together, these studies indicate that daily consumption of HFC by healthy adults in amounts that result in total cumulative intakes approximating up to 150% of the typical cumulative human exposure to Humifulvate is of no health concern.

Two groups of adults (18 total) and one group of 12 children being treated for acute or chronic lead poisoning have received the equivalents of 15% to 20% of the typical cumulative human exposure to Humifulvate with two reports of unspecified "mild side effects." [57,58]

A cohort of 60 children with a variety of illnesses, including iron deficiency anemia, alopecia, and eczema have been treated with daily doses of HFC of 50-mg/10 kg body weight for periods of 3 weeks to 6 months (equivalent to, 375 mg/day for a 75 kg adult, or up to 7.5 times the typical cumulative human exposure to Humifulvate). [61] One patient reported an allergic skin reaction and one patient reported diarrhea and other unspecified "abdominal complaints."

A cohort of 40 adults and children with malignant lymphoma were treated with oral HFC (adults: 156.7 mg/day; children: 78.4 mg/day) for unspecified lengths of time. [67] One patient reported nausea and a "general feeling of weakness." A cohort of 64 adults with cancerous tumors was treated with 156.7 mg/day of HFC for up to 18 months (equivalent to up to 9 times the typical cumulative human exposure to Humifulvate) with reports of epigastric pain in 6 patients, heartburn in one patient and stomach Complaints and nausea in 5 patients. [59] Another cohort of 10 adults with cancerous tumors has been treated with oral HFC at unspecified dosages for an average treatment period of 2.6 years without any reported adverse events or subject complaints. [60] Three patients with cancerous tumors received oral HFC (unspecified dosages) continuously for 5 years without adverse effect. [22,23]

These studies on clinical patients with lead poisoning, childhood ailments, malignant lymphoma and solid tumors indicate that oral HFC and its primary component, Humifulvate, are without significant adverse effect in such individuals in total exposures of up to 9 times the typical cumulative human exposure to Humifulvate.

HFC Metal Content of HFC

An independent laboratory analysis performed by Flora Research Laboratory (San Juan Capistrano, CA) in November, 1999, reported that HFC contains 20.7 ppm aluminum, 20.07 ppm arsenic, 0.02 ppm cadmium and 0.07 ppm lead. Based on these data, it can be estimated that a single daily dose of HFC would result in the ingestion of 180 mcg of aluminum, 0.6 mcg of arsenic, 1.8 mcg of cadmium and 0.6 mcg of lead.

Many sources of food can contain up to 10 ppm of aluminum and it has been estimated that at least 2 to 3 mg of aluminum are consumed by many people daily.[68] On this basis it can be concluded that the aluminum in a single dose of HFC could provide about 5% to 10% of an individual's typical daily exposure to oral aluminum.

The amounts of lead and arsenic contained in a single dose of HFC are well within the limits set by "Proposition 65" in the state of California, [69] standards for exposure to, heavy metals that are used by many manufacturers of dietary supplements to ensure the safety of their products.

Although cadmium has only an oral inhalation limit, data from one study has led to the conclusion that average daily cadmium intake should be kept below 111 mcg,[70] over 60 times the amount contained in a single dose of HFC. Average daily intakes of cadmium from food in most areas that are not polluted with environmental cadmium range between 10 mcg and 40 mcg,[71] 5 to 25 times the amount contained in a single dose of HFC. The FAO/WHO Expert Committee on Food Additives and Food Contaminants recommended a tolerable weekly cadmium intake of 400 mcg to 500 mcg for an adult, or a daily average of 64 mcg to 79 mcg (about 35 to 40 times the amount of cadmium contained in a single dose of HFC).

Absence of Polycyclic Aromatic Hydrocarbons in HFC

The National Institute of Food and Nutrition Science (OETI) in Budapest, Hungary, reported that it was unable to detect any polycyclic aromatic hydrocarbons in samples of HFC, including benzo-(a)-pyrene, benzo-(b)-fluoranthene, indeno(1,2,3-cd)pyrene, benzo-(k)fluoranthene, fluoranthene, or benzo-(ghi)-perylene.

Conclusion and Certification

The information and scientific studies referenced herein establish that the Humifultate, when used under the conditions recommended, is safe.

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