

New advice on safety of high doses of vitamins and minerals clarifies muddle

The safety of vitamin and mineral supplements generated a huge amount of media interest last week. Pharmacists may be wondering what advice they should give to confused consumers and which products they should stock. Pamela Mason, a pharmacist with a special interest in nutrition, reports

“VITAMINS can damage your health” warned one paper last week. “Too many vitamins can be bad for you,” said another.

The trigger for the media interest was the publication of the final report of the Expert Group on Vitamins and Minerals (EVM). The EVM is an independent advisory group, which consists of 11 members, including representatives of the scientific community, consumer organisations and industry. It was set up in 1998 to advise the Food Standards Agency (FSA) on the safety of vitamins and minerals used in food supplements or added to foods (ie, fortified foods). In August last year the group published a draft report which, following a consultation period, has now been modified to produce the final version.

The market for dietary supplements has grown enormously during the past 20 years and in the United Kingdom, 40 per cent of women and 30 per cent of men now take one or more of these products regularly. In the light of this increased usage, concern has been expressed as to the possible risks of taking high doses of vitamins and minerals, and the EVM was established in response to this concern. The group has made recommendations on 31 vitamins and minerals, which the FSA is now using to advise the public on levels of intake that are unlikely to cause any harm.

Commenting on the proposed EVM levels, Dr Ann Walker, nutrition lecturer at Reading University and adviser to the Health Supplements Information Service, says: “The most important outcome of this and other reviews of vitamins and minerals being carried out on a European-wide basis is that we can give clear, consistent and appropriate advice to the public on the use of vitamins and minerals.”

The Proprietary Association of Great Britain (PAGB) also welcomes the EVM report. Sheila Kelly, its executive director, comments: “The safety of the consumer must be our paramount concern. Manufacturers will take account of this new expert advice and the PAGB will work with the FSA to ensure we advise and educate consumers appropriately.”

However, the Health Food Manufacturers Association (HFMA) has some doubts. On its website it expresses regret that “in some cases the upper safe levels and guidance levels determined by the EVM differ significantly from those of other interna-

tionally recognised committees.” These include the Food and Nutrition Board of the US National Academy of Sciences and the European Commission’s Scientific Committee on Food. For example, the EVM levels for vitamin A and vitamin B₆ are lower than those set by these two other committees.

The HFMA has called for greater international collaboration “to seek to reach a

contained in licensed medicines. Vitamins and minerals present in medicines are with- in the remit of the Medicines and Health-care products Regulatory Agency.

HOW WAS THE GUIDANCE PRODUCED?

The EVM reviewed data on 34 vitamins, minerals and trace elements. Consideration was given to those either to be essential to human health or available in dietary supplements. The list therefore included trace elements such as nickel, vanadium and tin, which are found in supplements, but for which evidence of essentiality in humans is limited. Germanium was also considered; this is not known to be essential and has been withdrawn from the UK market due to toxicity, but supplements can still be obtained by mail order or on the internet.

Evidence for each substance was assessed according to a hierarchy. Thus, data from double-blind placebo-controlled trials in humans took precedence over data from animal studies. However, human trials with vitamins and minerals are usually designed to assess the beneficial effects of nutrients rather than their potential adverse effects. Animal studies are also frequently of a poor standard. Not surprisingly, the EVM concluded that current toxicity data for vitamins and minerals fall far short of that for licensed medicines. Another factor that the group had to grapple with was the huge variability in margins that exist between nutritional requirements and toxicity. Both of these factors created difficulties for the EVM in setting upper safety limits.

WHAT ARE THE SAFETY LIMITS?

The safety limits are complex and the figures in Table 1 should be read with care. Some of the figures refer to supplementary intake and some to total intake from foods and supplements. Some are safe upper levels (SULs), established where there were adequate data; other figures represent guidance on safe levels of intake because setting of SULs was not possible from the evidence available. Indeed, evidence was robust enough to establish safe upper levels for only eight of the 34 vitamins and minerals considered. These are vitamin B₆, vitamin E, beta-carotene, zinc, copper, selenium, boron and silicon. Guidance was issued for a further 22 nutrients: vitamin A, thiamin,

New guidance on the use of vitamins and minerals should allow pharmacists to advise customers about using different products

greater consensus so as to protect both consumer safety and the freedom to choose safe higher potency supplements”.

This new report is of particular relevance to pharmacists because they are often asked by the public whether or not it is safe to take two or more supplements together. For example, could a multivitamin taken with cod liver oil provide an amount of vitamin A that is potentially unsafe? Could a calcium and vitamin D tablet provide a daily intake of vitamin D that is too high when taken with a multivitamin?

Pharmacists are uniquely placed to provide such advice not only because they sell dietary supplements and are asked for advice about them, but also because they can have an important role in monitoring the safe use of these products. Pharmacists should encourage patients to tell them which, if any, vitamin products they are using. The upper safety limits identified in the EVM report (see Table 1) can then be used as a framework to provide guidance on the safety of the supplements the individual is taking or wants to take. These figures are relevant only to vitamins and minerals sold under food law (ie, those present in foods and food supplements) and not to those

ADRIENNE HART-DAVIES/SPSL

riboflavin, vitamin B₁₂, vitamin C, vitamin D, niacin, biotin, folic acid, pantothenic acid, calcium, iodine, iron, magnesium, phosphorus, vitamin K, chromium, manganese, molybdenum, cobalt, nickel and potassium.

The EVM considered the data insufficient to establish either SULs or guidance for germanium, vanadium, sodium and chlorine (sodium chloride). Germanium, the report says is not suitable for supplementation even though it is still available by mail order. Vanadium supplements in doses of 10–25mg daily are often targeted at body builders, but such doses may not be safe, the report warns.

It is important to be clear that both SULs and guidance levels are the doses of vitamins and minerals that individuals could take daily on a life-long basis without medical supervision. They are not recommended intakes but amounts that people should, on current evidence, be able to take without harm for long periods of time. In addition, guidance levels should not be confused with SULs. Guidance levels represent approximate levels that would not be expected to cause adverse effects but they are derived from limited data and are less secure than SULs.

The EVM report also points out that the SULs may be considerably lower than might be appropriate during medical treatment where the balance between therapeutic benefit and safe use can be monitored. For example, vitamin D caused by intestinal malabsorption or chronic liver disease usually requires vitamin D in pharmacological doses such as calciferol tablets up to 1mg daily (BNF 45, March 2003, p470), while the guidance on upper intakes of vitamin D from dietary supplements on a long-term basis is 25µg (see Table 1).

There is also a hint in the report that intakes higher than the SULs or guidance levels could be appropriate in the short term for specific indications as and when clinical research reveals benefits. However, the EVM does not specifically encourage this.

Following the publication of the report, the FSA said that current intakes of most vitamins and minerals are not thought to be harmful and that most supplements are safe. "However, taking some high-dose supplements over a long period could be harmful," said Sir John Krebs, chairman of the FSA.

A significant proportion of supplements are multivitamins and minerals that contain no more than 100 per cent of the RDA of a range of nutrients. The EVM's SULs and guidance intakes are in general far higher than RDAs. However, pharmacists should take care in their recommendations on supplements containing vitamin A. Taking a multivitamin and high doses of some cod liver oil products could provide an intake above the guidance level for vitamin A. For individuals wanting to take such a combination, a fish body oil supplement would be a safer option.

The situation is similar with vitamin D. Labels of, for example, calcium and vitamin D products should be studied carefully if these products are to be taken with a multi-

vitamin. In the majority of cases the combined supplemental intake will not exceed 20µg vitamin D.

Zinc is another one to watch out for. Many multivitamin and mineral supplements contain 15mg of zinc — the RDA — which is fine, but individuals may want to take zinc supplements for other purposes, for example, in the hope of preventing or treating colds (although the evidence is at best slim). Toxic effects of zinc include gastrointestinal symptoms, but these do not usually occur with doses under 200mg daily. Effects on copper metabolism can occur at lower doses, so the SUL of 25mg daily should not be exceeded for long periods.

The EVM report draws particular attention to chromium picolinate, which may have the potential to cause cancer. The advice is not to take chromium in this form. The FSA has consulted on a proposal to ban its use in the manufacture of food supplements. However, the report says that having 10mg a day or less in total of chromium in other forms is unlikely to cause any harm.

Other nutrients highlighted include vitamin C, which at high doses is often taken for prevention and treatment of colds. At levels exceeding 1,000mg a day, vitamin C can cause abdominal pain and diarrhoea. Some patient groups seem to be at particu-

lar risk from high vitamin C intake. These include those who are heterozygous for haemochromatosis and thalassaemia, or those with a predisposition to renal or urinary stones. The report points out that possible adverse effects in these individuals appear to occur at intakes above 1,000mg daily.

High intakes of calcium (above 1,500mg/day) and iron (above 17mg a day) may also result in gastrointestinal symptoms in some people. However, these symptoms should disappear once people stop taking the supplements. The FSA is also re-emphasising advice not to exceed a daily intake of vitamin B₆ from supplements of 10mg because of the risk of peripheral neuropathy. The SUL for beta-carotene has been set at 7mg daily because of the association between high intakes of this substance and lung cancer in smokers. The report adds that the effects of higher doses of beta-carotene in non-smokers are not known. The guidance given for manganese reflects the particular susceptibility of older people to higher doses of this trace element, and older people should be advised to avoid supplemental intake higher than 0.5mg daily.

The EVM report is available on the FSA website (www.food.gov.uk).

TABLE 1: GUIDANCE ON UPPER SAFE LEVELS OF VITAMINS AND MINERALS IN HEALTHY ADULTS

Vitamin/mineral	EU RDA*	Upper safe limits†
Vitamin A (retinol equivalent) (µg)	800	1,500 (G,T)
Vitamin B ₁ (thiamin) (mg)	1.4	100 (G,S)
Vitamin B ₂ (riboflavin) (mg)	1.6	40 (G,S); 43 (G,T)
Vitamin B ₆ (pyridoxine) (mg)	2	10 (U,S)
Vitamin B ₁₂ (cobalamin) (µg)	1	2,000 (G,S)
Vitamin C (ascorbic acid) (mg)	60	1,000 (G,S)
Vitamin D (cholecalciferol) (µg)	5	25 (G,S)
Vitamin E (tocopherol) (mg)	10	540 (U,S) (800 IU)
Vitamin K (µg)	—	1,000 (G,S)
Niacin (mg)	18	—
Nicotinamide (mg)	—	500 (G,S); 560 (G,T)
Nicotinic acid (mg)	—	17 (G,S)
Biotin (µg)	150	900 (G,S); 970 (G,T)
Folic acid (µg)	200	1,000 (G,S); 1500 (G,T)
Pantothenic acid (mg)	6	200 (G,S); 210 (G,T)
Calcium (mg)	800	1,500 (G,S)
Iodine (µg)	150	500 (G,S); 940 (G,T)
Iron (mg)	14	17 (G,S)
Magnesium (mg)	300	400 (G,S)
Phosphorus (mg)	800	250 (G,S); 2400 (G,T)
Potassium (mg)	—	3,700 (G,S)
Zinc (mg)	15	25(U,S); 42 (U,T)
Beta-carotene (mg)	—	7 (U,S)
Chromium (µg)	—	10,000 (G,T)
Copper (mg)	—	1 (U,S); 10 (U,T)
Manganese (mg)	—	0.5-4 (G,S); 8.7-12.2 (G,T)
Molybdenum (µg)	Level not set	
Selenium (µg)	—	350 (U,S); 450 (U,T)
Boron (mg)	—	6 (U,S); 9.6 (U,T)
Cobalt (mg)	—	1.4 (G, T)
Nickel (µg)	Level not set	
Silicon (mg)	—	700 (U,S); 760 (U,T)
Tin (mg)	—	13 (G,T)
Vanadium (mg)	Level not set	

* EU RDA — the Recommended Daily Allowance considered sufficient to prevent deficiency in most individuals in the population. The RDA is used on the labels of dietary supplements. The EU has not set RDAs for some nutrients

† Upper Safety Limits — these refer to the maximum amount of a vitamin or mineral that can be taken each day as a long-term supplement. U = Safe Upper Level set by the Expert Vitamin and Mineral (EVM) group. All levels marked (G) represent guidance only; S = intake from supplements alone. T = total intake from all sources including food and supplements