REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF ASTAXANTHIN IN FEEDINGSTUFFS FOR SALMON AND TROUT

Opinion expressed 8 March 1989

TERMS OF REFERENCE (June 1985)

The Scientific Committee for Animal Nutrition is requested to give an opinion on the following questions :

1. Does the use of astaxanthin at the level of 100 mg/kg of complete feedingstuff result in effects on the fish other than the pigmentation of the muscle and skin ?

2. Does the desired pigmentation need the use of 100 mg astaxanthin/kg complete feedingstuff throughout the rearing period ?

3. Is the proposed use safe for the target species ?

4. Is the proposed use safe for the consumer ? Which is the qualitative and quantitative composition of astaxanthin residues in edible tissues and organs of the fish ?

BACKGROUND

It is necessary to establish whether the use of astaxanthin under the proposed conditions is in conformity with the requirements of Council Directive 70/524/EEC of 23 November 1970 concerning additives in feedingstuffs (1) (2).

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(1) O.J. No. L 270 of 14.12.1970, p. 1

(2) O.J. No. L 319 of 8.12.1984, p. 13

OPINION OF THE COMMITTEE

1. Many species of crustacea and fish contain carotenoids naturally in their muscle and skin. However, only certain salmonid species have pigmented muscle. Astaxanthin is the major carotenoid of wild Atlantic salmon, while other salmonids may utilisé a wider range of carotenoids. Free astaxanthin and its isomers have been identified in the muscle of many sea and fresh water species of salmon. The carotenoids in the skin are usually esterifiéd. The source of all carotenoids in muscle and skin of salmonids is their food as the carotenoids cannot be synthesised by the fish. It is therefore necessary to add astaxanthin to salmon and trout feedingstuffs, when the fish are reared in fish farms to replace the natural sources. Astaxanthin occurs in the muscle of wild salmon and trout at levels up to 35 mg/kg. Because astaxanthin is the natural pigment in the muscle and skin of salmon and trout at levels higher than can be induced by feedingstuffs containing 200 mg/kg it cannot result in unforeseen biological effects.

2. The incorporation of 20-100 mg astaxanthin/kg complete feedingstuff over 15 days yields a level in the muscle of farmed salmon and trout of 3 and 8 mg/kg muscle respectively. 200 mg/kg feedingstuff produce about 10 mg/kg muscle and 400 mg/kg feedingstuff about 15 mg/kg muscle. To achieve a desirable colouring of the muscle, doses of 20 to 100 mg astaxanthin/kg complete feedingstuff need to be administered during the greater part of the growing period.

3. The data supplied show that astaxanthin is safe for salmonids. It may contribute to the development of fish and crustaceans and be involved in the physiology of the reproductive functions, like mating behaviour, stimulation of spermatozoa, protection of eggs against light etc. In a recent publication it has been reported that astaxanthin has a favourable effect on the immune reponse (3).

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(3) Bendich, A. and Shapiro, S.S., J. Nutrition, 116, 2254-2262, 1986
Al-Kalifa, A., Simpson, K.L., Comp. Biochem. Physiol.B. Comp. Biochem., 91 B, 563-568, 1988
Dossier from Hoffman-La Roche 1986

4. Astaxanthin has a low acute toxicity, the oral LD-50 being over 2000 mg/kg in the rat. A 14-week study in rats with doses of 300, 600 and 1200 mg/kg b.w. showed slight hepatotoxicity at the higher levels and some nephrotoxicity at the highest dose. The NEL was 300 mg/kg b.w. A 13-week study in dogs with doses of 40, 75 and 160 mg/kg b.w. showed no adverse effects.

A one generation reproduction study in rats with doses of 25, 100 and 400 mg/kg b.w./day showed no adverse effects on reproductive function. Litter parameters and pup development were normal except for a higher pup mortality during lactation at the highest dose level. The NEL was 100 mg/kg b.w. Embryotoxicity and teratogenicity studies in rats with doses of 250, 500 and 1000 mg/kg b.w. and in rabbits with 100, 200, and 400 mg/kg b.w. showed no adverse effects. There was no evidence of genotoxic potential in mutagenicity tests in Salmonella typhimurium and a micronucleus test in the mouse.

Because of the observation that moderately elevated doses of canthaxantin, a structurally closely related carotenoid, may cause retinal deposits of the carotenoid in the human retina, comparative studies on the metabolism and the pharmaco-kinetics of astaxanthin were carried out in the rat and man. Initial plasma levels of 14-C-labelled astaxanthin were much lower over the first 6 hours than those of equivalently dosed canthaxanthin but were subsequently similar. Canthaxanthin levels in the liver and spleen were much higher compared to astaxanthin, the highest levels of which were found in the small intestine. All other tissue levels remained comparable. Following a single oral administration only 10% was apparently absorbed, the remainder appearing in the faeces or gut contents, Of the absorbed astaxanthin some 66% appears in the urine, about 9% in the liver, about 7% in the gut and about 16% in the carcase. Astaxanthin is metabolised and excreted more quickly than canthaxanthin. About 10% of astaxanthin in feedingstuff is absorbed by fish, the proportion of isomers in the muscle matching that in the diet. No metabolism occurs in the muscle of fish but in the skin a small percentage is metabolised to zeaxanthin and other carotenoids.

Administration of 100 mg astaxanthin or canthaxanthin to a human volunteer resulted in almost 4 times higher peak plasma levels of canthaxanthin which would be equivalent to 7 kg fish containing 13 mg/kg astaxanthin. Astaxanthin was almost completely eliminated from the plasma after 48 hours while canthaxanthin levels had reduced to 50% only. After multiple administration the elimination half-time was about 17 hours for astaxanthin compared to 4.5 days for canthaxanthin. To reach similar steady-state plasma levels would require doses of astaxanthin 25 times higher than cantaxanthin.

The toxicity and pharmaco-kinetic data do not provide any evidence for a hazard to the consumer from the consumption of salmon or trout which had been fed up to 200 mg astaxanthin/kg complete feedingstuff. At this level of addition, the amount of astaxanthin appearing in the muscle of fish is about half that found in wild species. The question of residues or withdrawal periods therefore does not arise. The differences in the parmaco-kinetics of astaxanthin and canthaxanthin suggest that these compounds are metabolised differently by man. In addition man excretes astaxanthin much more rapidly so that retinal deposition of astaxanthin after consumption of pigmented fish muscle is unlikely. The use of astaxanthin up to 100 mg/kg complete feedingstuff is therefore acceptable in the opinion of the Committee.