INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

WORLD HEALTH ORGANIZATION

TOXICOLOGICAL EVALUATION OF SOME FOOD COLOURS, ENZYMES, FLAVOUR ENHANCERS, THICKENING AGENTS, AND CERTAIN FOOD ADDITIVES

WHO FOOD ADDITIVES SERIES 6

The evaluations contained in this publication were prepared by the Joint FAO/WHO Expert Committee on Food Additives which met in Rome, 4-13 June 1974[1]

World Health Organization Geneva 1975

[1] Eighteenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., 1974, No. 557. FAO Nutrition Meetings Report Series, 1974, No. 54.

MICROBIAL CARBOHYDRASE* (Aspergillus niger)

Explanation

This enzyme preparation has been evaluated for acceptable daily intake by the Joint FAO/WHO Expert Committee on Food Additives (see Annex 1, Ref. No. 27) in 1971.

Since the previous evaluation additional data have become available and are summarized and discussed in the following monograph. The previously published monograph has been expanded and is reproduced in its entirety below.

BIOLOGICAL DATA

BIOCHEMICAL ASPECTS

No information available.

TOXICOLOGICAL STUDIES

Special studies

Studies on sensitizing effect was tested on 20 albino guinea-pigs, 10 males and 10 females, of the Pirbright White strain by a challenge injection of 0.05 ml intracutaneous two weeks after 10 sensitizing injections of 1% Ultrazym 100 in a 2% carboxymethylcellulose solution. The challenge injection produced a more intense reaction than the sensitizing injections, indicating a skin sensitizing activity (Sachsse, 1971).

Acute toxicity

A 70% suspension of Ultrazym 100 in a 2% carboxymethyl-cellulose solution was dispersed over the shaved back of 12 RAC/f rats for 24 hours. Within 24 hours the rats of both dosage groups (1000 mg/kg and 2150 mg/kg) showed dyspnoea and lachrymation, but no skin irritation. Recovering after five days, no substance-related gross organ changes were observed at autopsy (Sachsse & Bathe, 1971b).

* This enzyme preparation is prepared from some varieties of Aspergillus niger.

Animal	Route	LD_{50} (mg/kg bw)	Reference
Mouse	Oral	>3 200	Hunt & Garvin, 1963
		>4 000	Hunt & Garvin, 1971
		>3 200	Willard & Garvin, 1963
		4 000	Garvin et al., 1966
Rat	Oral	10 000	Gray, 1960
		31 600	Kay & Calandra, 1962
		>3 200	Willard & Garvin, 1968
		>4 000	Garvin et al., 1966
		>10 000	Gray, 1960
Rabbit	Oral	>4 000	Garvin et al., 1966
Dog	Oral	>4 000	Garvin et al., 1966
Rat	Oral	7 750	Sachsse & Bathe (1971a)

Short-term studies

Rat

Four groups of 10 male rats received in their diet for 30 days

enzyme at 0, 0.5 and 5%. There were no adverse effects related to treatment regarding growth, appearance, behaviour, survival, food consumption, haematology, organ weights and gross pathology (Garvin et al., 1966).

Two groups of 10 male and 10 female rats received daily for 91 days in their diet either 0 or 5% enzyme. There was no difference from controls regarding appearance, behaviour, survival, weight gain, haematology, organ weights and gross pathology (Garvin & Merubia, 1959).

One group of 20 male and 20 female and four groups of 10 male and 10 female ARS Sprague-Dawley rats were fed 0, 5 and 10% carbohydrase (Wallerstein Pectinase Evaporate) and 5 and 10% carbohydrase

(Wallerstein Amylo glycosidase Evaporate) in the diet for 90 days (roughly equivalent to 3,5 and 7 g preparation/kg bw/day). Appearance and behaviour were normal, no deaths. Growth rate and food consumption were similar in all groups. No changes were seen in haematology and blood chemistry as compared with the respective controls. The relative weight of thyroid, liver and spleen in males and liver and spleen in females fed pectinase showed a dose-related decrease. The relative weight of liver in males and heart in females fed amyloglucosidase showed a tendency for dose-related decrease. Gross pathology and the only partly performed histopathology showed chronic pneumonia and renal tubular obstruction with hyalin casts, which did not seem to be dose related (Garvin et al., 1972).

Three groups of 10 male and 10 female Charles River rats were fed 0, 5 and 10% of Aspergillus niger mycelial preparation in their diet for 13 weeks. There were no overt signs of toxicity. Food consumption and growth were not affected. There was a drop in the efficiency of food utilization for both dosage groups and both sexes, which was significant for the high dose males. The haematological, the clinical and the ophthalmoscopic data, revealed no significant differences among the groups. There were significant increases in the relative kidney weight of females in both dosage groups. The gross and microscopic findings were mostly related to chronic respiratory disease and kidney lesions including hydropelvis or hydronephrosis, which did not appear to be treatment related (Swann & Cox, 1973).

Duckling

Groups of five ducklings received in their diet either 0, 1, 5 or 10% of enzyme for 29 days. Growth, feed consumption, behaviour and development were comparable in all groups. No gross liver lesions were seen at autopsy and mean liver weights were similar to controls. Histopathology of the livers was normal. No toxic element was noted (FDRL., 1963).

Mouse, Rat, Cat

Enzyme preparations from Aspergillus niger, strain "Pectolytic" produced by different cultivation methods were in several different acute and short-term studies given to a total number of 300 mice, 123 rats and 17 cats. The conclusion of the author is, that surface and deep culture preparations on media rich in sugars (sugar beet pulp, wheat bran) gave effects in some experimental animals after 45-750 mg/kg bw/day, of the different preparations mainly given in the drinking water. The main effects were decreased weight gain, increased leucocyte count, accelerated sedimentation of erythrocytes and abscesses different places in the body. A preparation isolated from the same mould, but cultivated on grain husk had no similar effects on the animals. The preparation methods are not described, especially is

not revealed whether the preparations were sterile (Magnova, 1968).

Long-term studies

None available.

Comments:

Aspergillus niger is a common contaminant of food. The available information indicates that it is not pathogenic to man. Duckling studies were done on two preparations and an adequate 90 days' study in rats is now available showing no toxicological effects at 10% in the diet. This meets the requirements as laid down by the Committee.

EVALUATION

Acceptable daily intake not specified.*

REFERENCES

FDRL (1963) Unpublished report No. 84600f submitted by Miles Chem. Co

Garvin, P. & Merubia, J. (1959) Unpublished report submitted by Baxter Laboratories Inc.

Garvin, P. J. et al. (1966) Unpublished report submitted by Baxter Laboratories Inc.

Garvin, P. J. (1972) Unpublished report No. R.D. 6 - 106 submitted by R. M. Gesler

Gray, E. H. (1960) Unpublished report submitted by Miles Laboratories Inc.

Hunt, R. F. & Garvin, P. J. (1963) Unpublished report submitted by Baxter Laboratories Inc.

Hunt, R. F. & Garvin, P. J. (1971) Unpublished report submitted by Travenol Laboratories Ltd

* The statement "ADI not specified" means that, on the basis of the available data (toxicological, biochemical, and other), the total daily intake of the substance, arising from its use or uses at the levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason, and for the reasons stated in individual evaluations, the establishment of an acceptable daily intake (ADI) in mg per kg of body weight is not deemed necessary.

Kay, J. H. & Calandra, J. C. (1962) Unpublished report submitted by Miles Chemical Co

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Phillips, B. M., Hartnagel, R. E. & Thompson, D. (1967) Unpublished report submitted by Miles Chemical Co

Sachsse, K. (1971) Unpublished report No. Siss 826 submitted by Ciba Geigy

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Swann, H. E. & Cox, G. E. (1973) Unpublished report laboratory No. 1223 submitted by Searle Biochemicals

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See Also:
Toxicological Abbreviations