Starch

(CAS reg no: 9005-25-8, 9005-84-9)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of starch by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by C de Heer, Ph.D. and H. Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of starch has been based on the review by the American Conference of Governmental Industrial Hygienists (ACGIH) (ACG99). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the online data bases Medline, Toxline and Chemical Abstracts covering the periods 1966 to 29 May 1998 (19980529/UP), 1965 to 24 February 1998 (19980224/ED), and 1967 to 2 June 1998 (980602/ED, vol 128, iss 23), respectively*. HSDB (no record) and RTECS, data bases available from CD-ROM, were consulted as well (NIO98, NLM98). The final literature search was performed in June 1998.

In July 2001, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	starch
synonyms	:	amylum, amicol, emjel 200, farinex, rice starch, cornstarch, W-gum, snowflake 30091
molecular formula	:	$(C_6H_{10}O_5)n$
structural formula	:	-
CAS reg no	:	9005-25-8 (starch); 9005-84-9 (soluble starch)

Data from ACG99, Ric94.

* The Medline search was performed using the search profile (((starch OR amylose OR amylopectin?) AND (TO OR PO OR AE OR CI)/CT) AND dust#) OR (((starch OR amylose OR amylopectin?) AND (TO OR PO OR AE OR CI)/CT) AND (air OR aero* OR respir*)) OR (((starch OR amylose OR amylopectin?) AND (TO OR PO OR AE OR CI)/CT) AND lung+NT/CT) OR (((starch OR amylose OR amylopectin?) AND (TO OR PO OR AE OR CI)/CT) AND lung diseases+NT/CT). In addition, the Medline database was searched with starch/CT(L)(AE OR PO OR TO)/CT AND (EN OR DE OR FR OR NL)/LA. Toxline was searched with ((starch OR 9005-25-8 OR 9005-84-9) AND 1996/PY) and ((9005-25-8 OR 9005-84-9) AND (1994 OR 1995/PY)). CA was searched with ((9005-25-8 OR 9005-84-9) AND 4/SC), ((9005-25-8 OR (9005-84-9) AND 59/SC AND health), and (9005-25-8 (L) toxic*). In addition, Toxline was searched with ((9005-25-8 OR 9005-84-9 OR 9037-22-3) AND (RISKLINE OR CIS OR NTIS OR TSCATS)/FS)) and ((9005-25-8 OR 9005-84-9 OR 9037-22-3) NOT (TOXBIB OR IPA OR BIOSIS)/FS). The search profile for CA was ((9005-25-8 OR 9005-84-9 OR 9037-22-3)/ADV).

3 Physical and chemical properties

Starch is a natural polysaccharide and a heterogeneous mixture of amylose and amylopectin which are linear and branched polymers of α-glucopyranosyl units, respectively. It is a soft, white, glistening powder that is tasteless and has no smell. Starch undergoes no change when exposed to the air. In cold water, starch absorbs water reversibly and swells slightly. In hot water, irreversible swelling occurs, producing gelatisation. The property of forming thick pastes or gels is the basis of many starch uses. Most starches are composed of 22-26% amylose and 74-78% amylopectin (ACG99, Ric94).

Soluble starch is made by treating potato or cornstarch with dilute hydrochloric acid.

4 Uses

Industrial uses of starch include the sizing of yarn and cloth in the textile industry, dressing cloth, printing, and mining. It is used in adhesives, explosives, cosmetics, glucose, corn syrups, and sugars for fermentation. Cornstarch, mixed with 2% magnesium oxide, is used as a donning powder in (surgical) gloves (ACG99, Ell90). Glove starch powder is comprised of corn- or maize starch powder partially cross-linked with epichlorohydrin and (up to 2.0%) magnesium oxide as dispersing agent (Pel86, She84).

Food products containing starch are made from rice, corn, and arrowroot, either alone or in food preparations requiring thickening, gelling, or similar properties. Starch is also used in laundry starch preparations and has been employed in the clinical management of acute iodine poisoning (ACG99).

5 Biotransformation and kinetics

No data were found.

Although percutaneous absorption of cornstarch has been suggested (Seg90), it is not likely to occur to a great extent in view of its molecular size. Data on absorption of starch after intraperitoneal administration are conflicting. Complete absorption was reported after studies in rats and dogs (Ell90, Tal88), yet other studies in the same species reported the development of granulomatous lesions after intraperitoneal administration of starch (Ell90). In rats, autoclaved starch

was almost totally absorbed from the peritoneal cavity within 48 hours, whereas irradiated starch was still not fully absorbed after a period of 70 days. This difference was suggested to be induced by the sterilisation method used, as scanning-electron microscopic studies on autoclaved starch showed that the surface of the granules was pitted and cracked, while similar studies on irradiated material showed a smooth surface (Ell94, Woo97).

6 Effects and mechanism of action

Human data

Skin contact with a total dose of 300 µg of starch, intermittently applied over a 3-day period, resulted in a mild erythema and slight oedema of the skin in humans (ACG99).

Dermatitis, anaphylactic reactions, and respiratory problems have been reported by workers who wear gloves as means of personal protection. Many reports describe allergic responses, both in skin and airways, after the use of latex and vinyl gloves with cornstarch glove powder. However, in nearly all cases the allergic responses were specific for latex proteins, which were shown to adhere to the glove powder, and not to cornstarch itself (ACG99, Ham93, Lun95, New97, Pis94, Tom94, Wra94). Responses to cornstarch not contaminated with latex proteins are extremely rare, but have been reported (Fis87, Seg90, Wra94). Contact urticaria, due to sensitivity to spray starch, was not caused by cornstarch but by other ingredients of the spray (McD79). Some workers may develop a chronic occupational dermatitis through the handling of starch products (ACG99).

Acute respiratory effects after exposure to dust from the refining process of potato starch have been described (personal sampling: 3.9-56.0 mg/m^3, total dust). The responsible agent could not be identified although the authors suspected endotoxin to be the causative agent (Hol94). Millers and bakers occupationally exposed to grain and flour dusts (personal sampling: 1.1-14.3 mg/m^3, total dust) showed significantly higher incidences of coughing and chronic bronchitis compared to a non-exposed reference group (Mas95, Mas96). A dose-response relationship was observed between dust exposure levels and chronic respiratory symptoms (Mas95). Although flour is a complex product that is mainly made up of starch (70%) and gluten (12%), it may also contain mite dust and endotoxins. The causative role of starch in the observed respiratory symptoms is therefore not clear. Community outbreaks of asthma associated with

inhalation of starch-containing soybean dust in Spanish harbors have been ascribed to low-molecular weight proteins of the hull of the soybean rather than to starch (Alv89, Ant89). Normally, starch dust is not considered harmful to the lungs although it may aggravate existing pulmonary disease such as emphysema (ACG99).

Epidemiologic data are inconclusive as to whether high-starch diets confer an increased risk for the development of stomach and pancreas cancer (Voi87, Kon96). The same holds true for hypothesised protective effects of high-starch diets (Bin88, Mun94, Ric94). In a two-period, placebo-controlled crossover study with periods of 7 days and a 7-day washout period between treatments, daily consumption of 45 g starch (in the form of native amylomaize supplemented to regular food) was well tolerated by healthy volunteers (Mun94).

A craving for starch (amylophagia) during pregnancy has no adverse effect on the fetus *per se*; however, chronic compulsive eating of starch, including daily ingestion of up to several pounds per day, contributes to iron deficiency anaemia, parotid hypertrophy, and intestinal obstruction (ACG99).

The use of modified starch as a surgical-glove lubricant can result in postoperative inflammatory reactions (*e.g.*, "starch peritonitis") and subsequent granulomatous disease in patients, caused by the presence of minute, accidentally introduced, quantities of glove powder (Car87, Ell90, Ell94, Kli90, Tow94, Woo97). It was found that in contaminated wounds, cornstarch enhanced the growth of bacteria and elicited exaggerated inflammatory responses as measured by wound induration (Ruh94, Woo97).

Animal data

Delayed type hypersensitivity reactions to starch could be induced in guinea pigs inoculated intradermally with starch and Freund's adjuvant. When these immunised guinea pigs were challenged with an intraperitoneal injection of 10 mg of starch in saline solution, florid omental granulomas developed in 8 of 36 animals. The remaining immunised animals, and the controls, showed only a low grade microscopic inflammatory reaction (Ell90, Woo97).

The intraperitoneal LD_{50} of starch in mice is 6600 mg/kg (ACG99).

Male rats given starch as a 60% (w/v) paste in distilled water by gavage for 14 consecutive days at levels up to 168 g/kg bw/day showed little, if any, signs of intoxication. In these animals, water was absorbed from the paste in the stomach and upper bowel, and the starch was converted to a calculus. Probably as a result, considerable hypertrophy of the smooth muscle of the

gastrointestinal tract was seen after 14 days of exposure. A subsequent increment of the daily dose for 2-7 weeks resulted in some inhibition of growth at dose levels of 10% of body weight. At dose levels of 20% of body weight, increased susceptibility to pneumonia and bowel obstruction owing to the inability of the animal to evacuate the starch calculi were observed (Boy68).

Male Wistar rats (n=10) fed diets containing 71% of different starches as dietary carbohydrate for 3 weeks showed no indications of short-term toxic effects. When 16% raw potato starch was added to 55% maize starch, a marked increase in caecal weights was noted relative to animals receiving only maize starch (71%). Marked thickening of caecal mucosa and submucosa were noted at histological examination. In addition, lymphatics were prominent, and there were indications of hypertrophy of the musculature and slight oedema of the mucosa and submucosa. It is noted by the authors that raw potato starch is relatively resistent to pancreatic amylase (Wal78).

"Half a teaspoon" of starch placed into the peritoneal cavity of 10 dogs was completely absorbed without any inflammatory reaction after 3 weeks (Ell90). In another experiment, 1 gram of starch produced few nodules within the peritoneal cavity of 2 of 12 dogs (Ell90). In subsequent studies in dogs, it was shown that granulomas and adhesions could develop especially when large clumps of starch were present. The presence of minimal peritoneal trauma may lead to adhesions (Ell90, Woo97). Granulomatous reaction to intraperitoneal glove starch powder was also shown in mice, rats, guinea pigs, and rabbits (Ell90, Nor87, Pel86, Pet86, She84). In rats, injection of starch granules failed to produce granulomas. After implantation of food particles of plant origin in rats as a model for human oral pulse granuloma, the starch component was readily digested leaving the cellulose fraction which invoked the granulomatous response (Tal88).

Microspheres of starch injected into a small segment of one lung of mice caused both lungs to become oedematous (Gre70).

A long-term study was carried out on the effects of inoculating 1.5 g of starch powder into the peritoneal cavity of rats. After an initial considerable inflammatory reaction, the intense vascular reaction subsided, leaving firm adhesions that were still present in animals sacrificed at 18 months (Ell90).

Feeding of unmodified cornstarch and potato starch to groups of rats at dietary levels up to 30% (equivalent to 27.4-33.6 g/kg bw/d) in a 2-year test and 10% (food intake not indicated) in a 3-generation test did not result in distinct toxicologically significant effects (Gro74). Rats fed a cooked diet containing 62% unmodified maize starch (equivalent to 51.1 g/kg bw/d*) for 2 years also did not

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* Calculation based on indicated food intake and body weights of wk 1-4 of the experiment

show significant toxicological effects, including reproductive effects over 3 generations (Tru79). Slight growth retardation was seen in rats exposed for 4 weeks to raw potato starch at a dietary level of 40% (equivalent to 46.0-52.8 g/kg bw/d) (Fer73).

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for starch in the Netherlands is 10 mg/m^3, 8-hour TWA, equal to the occupational exposure limit for nuisance dust.

Existing occupational exposure limits for starch in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

Skin contact with a total dose of 300 g of starch, intermittently applied over a 3-day period, resulted in a mild erythema and slight oedema of the skin in humans.

Airborne cornstarch powder from latex gloves can be a respiratory occupational hazard. Dermatitis, anaphylactic reactions, and respiratory problems have been reported by workers who don (latex) gloves as means of personal protection. However, latex proteins absorbed by the cornstarch powder and not the cornstarch itself was the causative agent of the respiratory problems in most, if not all, workers. Cornstarch is an extremely rare sensitiser.

Occupational exposures of potato starch industry workers and of grain and flour mill workers to starch-containing dusts resulted in acute respiratory effects. Because of combined exposures, the relative contribution of starch to the reported health problems could not be evaluated.

It may be possible that starch depositing in damaged skin or respiratory tract tissue leads to the development of granulomatous reactions.

There were no indications for significant toxicity, carcinogenicity or reproduction toxicity of starch in rats fed 27.4-52.8 g/kg bw/day.

The committee considers the toxicological data base on starch too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that there is insufficient information to comment on the level of the present MAC-value.

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Annex

Occupational exposure limits for starch in various countries.

country -organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	lit ref[b]
	ppm	mg/m^3				
The Netherlands						
-Ministry of Social Affairs and Employment	-	10[c]	8 h	administrative		SZW01
Germany						
-AGS	-					TRG00
-DFG MAK-Kommission	-					DFG01
Great-Britain						
-HSE	-	10[c]	8 h	OES		HSE01
	-	5[d]	8 h	OES		
Sweden	-	-		-		Arb00b
Denmark	-	-				Arb00a
USA						
-ACGIH	-	10[c]	8 h	TLV	A4[f]	ACG01
-OSHA	-	15[e]	8 h	PEL		ACG00
	-	5[d]		PEL		
-NIOSH	-	10[e]	10 h	REL		ACG00
	-	5[e]		REL		
European Union						
-SCOEL	-	-				CEC00

[a] S = skin notation; which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation

[b] Reference to the most recent official publication of occupational exposure limits

[c] (Total) inhalable dust

[d] Respirable dust

[e] Total dust

[f] Classified as A4 carcinogen, *i.e.*, not classifiable as a human carcinogen: agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories