



A 90-day oral (dietary) toxicity and mass balance study of corn starch fiber in Sprague Dawley rats



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ABSTRACT

The potential toxicity of corn starch fiber was assessed and compared to polydextrose, a commonly used bulking agent with a long history of safe use in the food supply. Groups of male and female CrI:CD(SD) rats were fed 0 (control), 1,000, 3,000, or 10,000 mg/kg-bw/day corn starch fiber in the diet for 90 days. The polydextrose reference article was offered on a comparable regimen at 10,000 mg/kg-bw/day. Following a single gavage dose of [¹⁴C]-corn starch fiber on study day 13 or 90, the mass balance of the test article was assessed by analysis of excreta samples collected from 0 to 168 h post-dose. There were no toxicologically or biologically relevant findings in any of the test article-treated groups. The few minor differences observed between the corn starch fiber and polydextrose exposed groups were considered to be due to normal biological variation. Following [¹⁴C]-corn starch fiber dosing, nearly complete excretion of the administered dose occurred over 168 h post-dosing, with the majority excreted in the feces. The dietary no-observed-adverse-effect level of corn starch fiber after 90 days was 10,000 mg/kg-bw/day. Similar toxicity profiles for corn starch fiber and polydextrose were observed due to the structural and compositional similarities of these materials.

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1. Introduction

Corn starch fiber is a novel dietary fiber produced via a polycondensation reaction from dextrose syrup and an acid catalyst. The result is a gluco-oligosaccharide composed of random 1–2, 1–3, 1–4, and 1–6 glc-glc bonds (1–6 glycosidic linkage predominates) (Fig. 1). Corn starch fiber is intended as a replacement ingredient for products that use corn syrup and other nutritive sweeteners, resulting in reduction of sugar and calorie content while maintaining digestive tolerance. In addition, lower production cost, better stability in formulated foods and beverages, and

superior functional properties (e.g. low molecular weight and narrow molecular weight distribution) give corn starch fiber technical advantages compared to other commercially available bulking agents such as polydextrose. Polydextrose is a 1 kcal/g glucose polymer produced under a thermal vacuum in the presence of a food acid catalyst, using sorbitol as a plasticizer (Craig et al., 2000). Random polymerization gives a highly branched structure in which the 1,6 bond predominates. Polydextrose has an average degree of polymerization (DP) of 12 and a molecular weight distribution of approximately 89% MW 162–5000 (Craig et al., 2000; Stumm and Baltes, 1997). In comparison, corn starch fiber has an average DP of 9.2 and a molecular weight (MW) distribution of approximately 99% MW 162–5000 (Cargill, Inc.; unpublished data on-file).

In addition to the above-mentioned technical improvements for corn starch fiber product applications, consumer acceptability of corn starch fiber is also anticipated to be higher relative to an ingredient like polydextrose which is produced using a polyol and may be negatively associated with gastrointestinal effects. The

Abbreviations: AAALAC, Association for Assessment and Accreditation of Laboratory Animal Care; ANOVA, analysis of variance; FDA, United States Food and Drug Administration; HPLC-CAD, high performance liquid chromatography - charged aerosol detection; IACUC, Institutional Animal Care and Use Committee; LSC, liquid scintillation counting; NOAEL, no-observed-adverse-effect level; OECD, Organisation for Economic Cooperation and Development; WBC, white blood cell.

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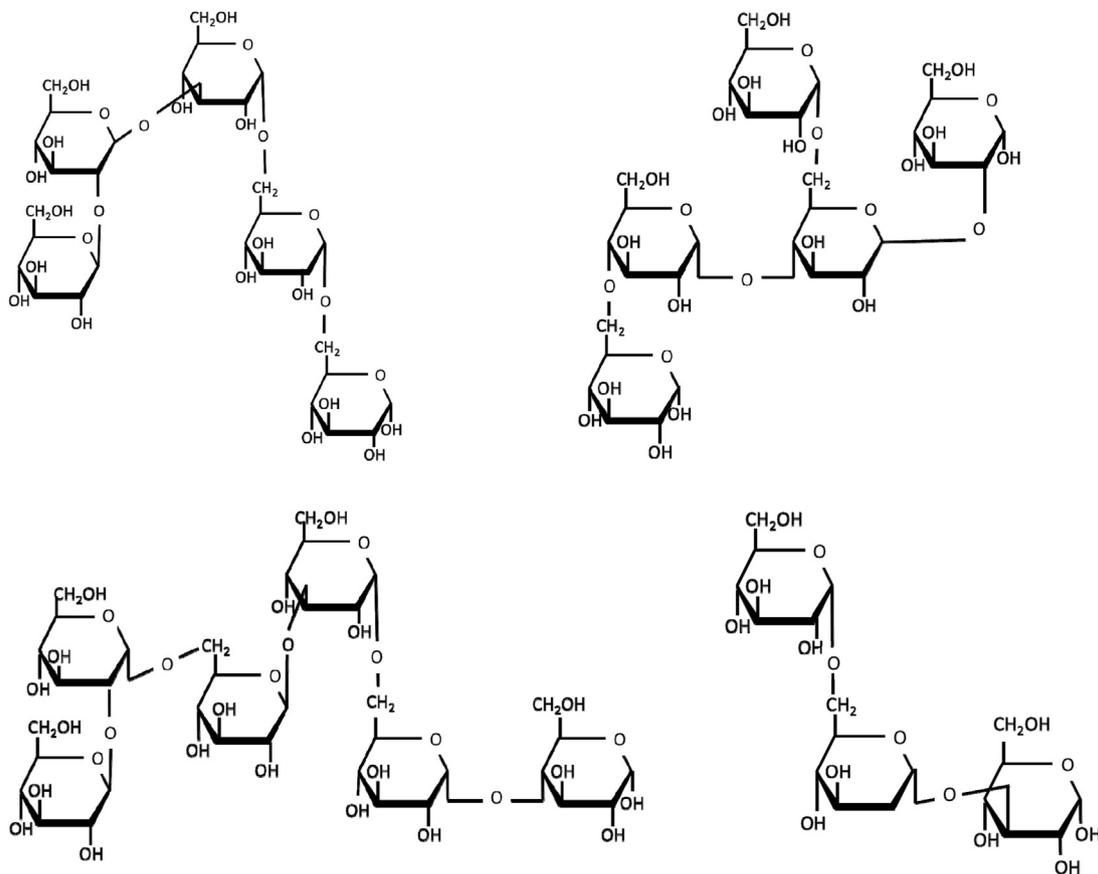


Fig. 1. Chemical structure for corn starch fiber.

gastrointestinal tolerability of corn starch fiber was confirmed in two acute studies using human volunteers (Crincoli et al., 2016), one providing a single serving of the novel dietary fiber and the other spreading the intake of the novel dietary fiber into four eating occasions over the course of one day.

In the present study, the toxicity of the reduced sugar/calorie bulking agent, corn starch fiber, was evaluated in a 90-day dietary study in Sprague Dawley rats. The potential toxicity of corn starch fiber was also compared to a reference article, polydextrose, which is a commonly used bulking agent with a comprehensive toxicology database and a long history of safe use in the food supply (Burdock and Flamm, 1999). This study was conducted at Charles River Laboratories (CRL) Ashland, LLC (formerly WIL Research), Ashland, Ohio, USA during July to October 2014. This study was conducted in compliance with FDA Good Laboratory Practice Regulations (21 CFR Part 58) (FDA, 1987), and in general accordance with U.S. Food and Drug Administration (FDA) Redbook Guideline IV.C.4.a. “Subchronic Toxicity Studies with Rodents” (FDA, 2003) and the Organisation for Economic Cooperation and Development (OECD) Testing Guideline No. 408 “Repeated Dose 90-day Oral Toxicity Study in Rodents” (OECD, 1998).

2. Materials and methods

2.1. Experimental design overview

The test article, corn starch fiber, was offered in the diet daily for a minimum of 91 consecutive days to Sprague Dawley rats. The reference article, Litesse II Polydextrose, and a concurrent negative control, basal diet, were offered on a comparable regimen. Six

additional animals/sex in Group 4 were transferred to the mass balance phase on study day 13 or 90. Radiolabeled corn starch fiber (also known as [^{14}C]-corn starch fiber) in the vehicle was administered orally by gavage to three mass balance animals/sex/day on study day 13 or 90. Animal allocation to dosage groups is summarized in Table 1.

Clinical examinations were performed daily and detailed physical examinations were performed weekly. Individual body weights and food consumption were recorded weekly. Ophthalmic examinations were performed prior to test diet administration and on study day 88 (Week 12). Clinical pathology evaluations were performed on all rats on study days 14 and 45 and prior to necropsy. Complete necropsies were conducted on all animals, and selected organs were weighed. Selected tissues were examined microscopically from all animals.

In the mass balance phase, after dose administration of [^{14}C]-corn starch fiber on study days 13 or 90, the mass balance animals were placed in individual metabolism units for separate collection of expired air and/or excreta components through 168 h following dose administration. Following the final excreta collection (study days 13 or 90), all mass balance animals were euthanized, weighed, and the carcasses were retained for possible future analysis. Aliquots of each sample type as well as the study day 90 female carcasses were analyzed for radioactivity.

2.2. Test article, reference article, and negative control diet

2.2.1. Test article and preparation of diets

The test article, corn starch fiber, (approximately 80% solids; 20% water) was supplied by Cargill, Incorporated. The reference article,

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