



DOSSIER · SUBSTANCE

Sorbitol

Independent efficacy studies on Sorbitol itself are rare. The most striking finding: In a large proportion of the frequently cited human studies, Sorbitol is not the test substance but a component of a formulation or a pretreatment.

112

STUDIES IN
TOTAL

30

IN HUMANS

13

OF WHICH
CONTROLLED

16

IN ANIMALS

10

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Sorbitol at a Glance

ORIGIN:
Sorbitol (D-Sorbitol) belongs to the sugar alcohols (polyols) and is not a sugar in the narrower sense, but a hexavalent alcohol that is formally derived from glucose. In metabolism, it stands in the polyol pathway: aldose reductase converts glucose to sorbitol, which is further metabolised to fructose. In application-related contexts, it appears in foods, chewing gums and pharmaceutical forms such as nasal spray, lozenge and bowel cleansing solution.

EVIDENCE BASE:
112 evaluated studies · 13 controlled studies in humans · 17 observational studies · 3 review articles · 16 animal experiments · 9 cell culture studies

- STRONGEST EVIDENCE:**
- **Inflammatory processes:** The systematic review of 2022 on sugar-free polyol chewing gums bases the sorbitol statement on a single study; it shows a small reduction in gingival scores versus the controls.
 - **Bitterness:** The randomised, single-blind, placebo-controlled crossover study of 2024 with 20 adults with schizophrenia showed a significant improvement in asenapine bitterness by D-sorbitol (p = 0,038).
 - **Plaque pH:** In the double-blind crossover study of 2024 with 16 adults, a 10-per-cent sorbitol solution did not alter the plaque pH value; sucrose lowered it from 7,0 ± 0,4 to 5,1 ± 0,1.
 - **Metabolism:** The 2021 review on sugar alcohols in diabetes reports that a portion of the sugar alcohols does not raise the plasma glucose level and calls for studies on toxicity and adverse effects.
 - **Cardiovascular:** In the observational analysis from POUNDS Lost, a combined sum score of mannitol and sorbitol was examined; higher baseline values of this sum score were associated with higher estimates of the 10-year risk for atherosclerotic cardiovascular disease; an independent contribution of sorbitol alone cannot be derived from this.

- LIMITATIONS:**
- In many frequently cited human studies, sorbitol is not the test substance but a component of a formulation or pretreatment; no contribution of the individual substance can be derived from this.
 - The 2025 review on xylitol chewing gum uses sorbitol throughout as the comparator arm; it measures the distance between xylitol and sorbitol, not the effect of sorbitol.
 - No therapeutic indication area is emerging; a large part of the studies originates from basic research, animal studies and cell culture, only a portion reaches humans.

CLASSIFICATION:
Sorbitol is a sugar alcohol of the polyol pathway that has been examined in humans primarily as a formulation or comparator component; independent efficacy investigations are at an early stage.

1. What Sorbitol Is

Sorbitol, almost always listed in the literature as D-sorbitol, belongs to the group of **sugar alcohols** (polyols). It is not a sugar in the narrower sense, but a hexavalent alcohol that is formally derived from glucose. In metabolism, it occupies a central position in the **polyol pathway**: the enzyme **aldose reductase** converts glucose to sorbitol, which is subsequently further metabolised to fructose. Two studies mention this pathway in the title — one examines the role of aldose reductase in glycosylation, the other the significance of fructose formed via the polyol pathway for growth and survival of tumour cells. In application-related literature, sorbitol appears predominantly in two roles: as a sugar alcohol in foods and chewing gums and as a component of pharmaceutical forms such as nasal spray, lozenge and bowel cleansing solution.

Decisive for the interpretation of all studies is the role in which sorbitol appears. In one part of the human studies, a **pretreatment with D-sorbitol** is examined to influence the bitterness of another active substance. In another part, sorbitol is a component of a formulation, for example a nasal spray containing carrageenan and sorbitol or a bowel cleansing solution made from D-sorbitol, ascorbic acid and picosulfate. Such studies examine the respective medicinal product, not sorbitol. Added to this is the range of investigation levels: a large part of the studies originates from **basic research**, **animal studies** and **cell culture**, only a portion reaches humans. Laboratory findings such as the inhibition of biofilms of Streptococcus mutans and Candida albicans by xylitol and sorbitol, which sucrose attenuates, are **preclinical** and cannot be transferred directly to use in humans.

2. What the Studies Show in Detail

The supporting human studies and the most important reviews — by application area, with population, duration, preparation, measured variable and result, as the original studies report them. Numbers appear only where the study states them.

Distribution of the **controlled studies in humans** by application area — the numbers are not additive, as one study may be assigned to several areas:

APPLICATION AREA	CONTROLLED STUDIES
Safety and tolerability	5
Uptake and availability	4
Metabolism	3

APPLICATION AREA	CONTROLLED STUDIES
Gut and microbiome	3
Immune system	2
Viral infections	2
Heart and circulation	1
Inflammatory processes	1

Inflammatory Processes

The systematic review of 2022 on the effect of sugar-free polyol chewing gums on gingival inflammation evaluated prospective randomised controlled clinical studies from 1971 to 2021. The initial search yielded 46 studies on erythritol, 102 on xylitol, 23 on sorbitol and nine on maltitol; after inclusion and exclusion, seven xylitol, one sorbitol and one maltitol study of high or acceptable quality remained. For sorbitol, the statement of this review therefore rests on a single included study. The abstract of the review provides no information on participant numbers, chewing time or intake quantity. Open question: a sufficiently large study on sorbitol-sweetened chewing gums with standardised chewing time, intake quantity and a gingival index as the primary endpoint.

This single sorbitol study shows a small reduction in gingival scores for sorbitol chewing gum versus the controls. For xylitol the basis is broader: in five of seven xylitol studies the gingival scores decreased, in two studies versus a polyol chewing gum and in three studies versus no chewing gum or a chewing-gum base. The authors conclude that habitual xylitol chewing-gum use can reduce gingival inflammation and, because of the small number and heterogeneity of the studies, consider further well-controlled investigations necessary. **Hypothesis:** The difference between xylitol and sorbitol in this review could also be due to the number of available studies and not to the two substances themselves. Whether sorbitol would perform similarly at comparable study density remains open.

Further Investigations

The 2025 review on xylitol chewing gum, mutans streptococci, plaque and caries ³¹ examined clinical studies in which xylitol chewing gum was compared with a polyol control gum containing sorbitol; included were prospective randomised or controlled studies up to 2025. From 908 titles on mutans streptococci, 879 on plaque and 658 on caries, 16 papers on mutans streptococci, ten on plaque and five on caries were evaluated after applying the criteria. In 12 of 14 studies xylitol chewing gum significantly lowered bacterial counts compared with sorbitol gum; plaque decreased in 6 of 10 studies and caries incidence in 3 of 5 studies, each versus sorbitol or sorbitol-containing gum. Three studies on mutans streptococci or plaque used a maltitol chewing-gum control; their results were contradictory. Sorbitol does not serve consistently as a comparator arm; the work measures the difference between xylitol and sorbitol, not the effect of sorbitol.

Two studies with D-sorbitol address the bitterness of asenapine. The randomised, single-blind, placebo-controlled crossover study from 2024 ⁷ included 20 adult patients with schizophrenia who rinsed once with D-sorbitol or placebo before each asenapine administration. D-sorbitol significantly improved bitterness ($p = 0.038$); willingness to continue asenapine did not increase significantly ($p = 0.180$) but showed improvement. The planning document published in 2023 ³ describes the same approach with 20 adult patients with schizophrenia-spectrum disorder in two groups of 10 each, who rinsed with both liquids one day apart. Both endpoints are questionnaires. Whether the reduced bitterness actually leads to better adherence remains the open question.

The 2022 observational study on vitamin status in hereditary fructose intolerance examined 32 patients with confirmed fructose intolerance and 32 healthy controls matched for age and sex. Lifelong treatment consists of a diet restricting fructose, sucrose and sorbitol. In 96.7 percent of affected individuals vitamin C intake and in 90 percent folate intake fell below the recommended reference intake; up to 69 percent received vitamin C and 50 percent folic acid as supplements. 15.6 percent showed vitamin C deficiency and 3.1 percent folate deficiency. Vitamin C intake and plasma levels correlated positively ($R = 0.443$; $p = 0.011$). Non-supplemented affected individuals were more frequently deficient than supplemented individuals (30 percent vs. 9.1 percent; $p = 0.01$) and than healthy controls (30 percent vs. 3.1 percent; $p < 0.001$). Sorbitol appears here as a component of the diet to be avoided, not as an investigated substance; statements about its effect cannot be derived from this. The survey is cross-sectional and concerns a rare disease.

The double-blind crossover study from 2024 with 16 adults ⁵ tested plaque pH after four interventions separated by seven days each: a 10-percent sucrose solution, a 10-percent sorbitol solution, a lozenge with nanohydroxyapatite, and a sucrose dose followed by a lozenge. Sorbitol did not change plaque pH. Sucrose lowered it from 7.0 ± 0.4 to a nadir of 5.1 ± 0.1 at minute seven; the critical threshold of 5.5 was crossed at minute twelve and the baseline value was not regained until after more than 30 minutes. The lozenge raised plaque pH within 30 minutes from 7.0 ± 0.3 to 7.8 ± 0.2 ; after a sucrose dose it rose with the lozenge to 5.5 in eight minutes and to baseline in 24 minutes. Sorbitol serves here as a comparator liquid; plaque pH is a surrogate endpoint and clinical outcomes such as caries were not recorded.

Viral Infections

They were exposed to grass pollen under controlled conditions and randomised to either a carrageenan- and sorbitol-containing nasal spray or saline; after one week they repeated the exposure with the alternate treatment. The primary endpoint was the mean change in the nasal congestion score; secondary endpoints included nasal airflow, nasal secretion and total symptom scores for nose, eyes and airways. Preclinical investigations showed barrier formation, virus blockade and water-withdrawing effects of the components; such an effect has not been investigated in humans. The clinical study found no significant difference in the mean change of the congestion score between spray and saline; nasal airflow increased. The tested spray contains two named components, so no effect of sorbitol alone can be derived from this work.

The second study, also published in 2024 ⁸, tested the same carrageenan- and sorbitol-containing nasal spray in adults with severe seasonal allergic rhinitis exposed to grass pollen for a total of six hours; the spray or saline was given after one hour and 45 minutes of exposure, followed one week later by the alternate treatment. Preclinical investigations report a virus-blocking, barrier-forming and water-withdrawing effect for the components; such an effect has not been investigated in humans. Both studies test a combination product of carrageenan and sorbitol; the role of sorbitol in the observed effects requires a design that compares the components individually.

Metabolism

The 2021 review on sugar alcohols as adjunctive measures in diabetes ¹⁰ considers xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt and erythritol and evaluates physical and chemical properties, metabolism, absorption as well as glycaemic and insulinaemic responses. Some sugar alcohols do not raise plasma glucose because they are only partially digested and metabolised. The authors see advantages for the treatment of hyperglycaemia but point to possible side effects at usual or higher intakes, recommend alignment with Food and Drug Administration guidelines and call for studies on possible toxicity and side effects. A uniform clinical endpoint is lacking and the tolerable amount has not been conclusively clarified.

The two-year weight-loss study POUNDS Lost was evaluated in an observational analysis ¹. In adults with overweight or obesity, erythritol, arabitol/xylitol and mannitol/sorbitol were measured in plasma at baseline (n = 802, 805 and 803) and after six months; changes were calculated in participants with both measurements (n = 664, 669 and 668). Higher baseline values of erythritol (β per 1 SD 1.1 percent [SE 0.2 percent]), arabitol/xylitol (β 1.3 percent [0.2 percent]) and mannitol/sorbitol (β 1.1 percent [0.2 percent]) were associated with higher estimates of 10-year risk for atherosclerotic cardiovascular disease. Mannitol and sorbitol were analysed as an isomer group, so the contribution of sorbitol alone cannot be read from this analysis and the work remains an observational association. Whether altered intake shifts plasma levels and thereby risk is an open question.

The 2025 review on chronic idiopathic axonal neuropathy ⁶ highlights two genetic causes that question the idiopathic classification: biallelic mutations in the sorbitol dehydrogenase gene SORD and repeat expansions in the RFC1 gene. SORD mutations are considered a leading cause of recessive axonal neuropathies and are linked to sorbitol accumulation and neurotoxicity; aldose reductase inhibitors are being investigated as possible therapy. RFC1 expansions are a major genetic contributor to CANVAS syndrome and sensory neuropathies. In addition, some patients with small-fibre neuropathy show autoantibodies against TS-HDS, FGFR-3 and plexin D1, indicating immune-mediated pathology; a randomised trial with immunoglobulins was negative. Sorbitol appears here as a metabolite that accumulates in SORD deficiency; which patients benefit clinically from lowering this accumulation remains open.

Another paper treats sorbitol as a metabolite rather than an ingested substance. The tracer metabolomics study from 2023 ¹¹ shows that disturbed polyol metabolism occurs not only in diabetes but also in PMM2-CDG, a congenital disorder of glycosylation. PMM2 deficiency alters intracellular glucose flux and increases polyol formation; inhibition of aldose reductase with epalrestat lowered polyols and raised GDP-mannose in patient-derived fibroblasts and in pmm2-mutant zebrafish and redirected glucose flux from polyol formation to nucleotide-sugar synthesis and thereby to glycosylation. These findings are preclinical; an effect in humans has not been investigated.

Immune System

The randomised, blinded six-month study from 2024 ²⁶ enrolled 250 children aged 1 to 5 years who did not use xylitol or sorbitol at baseline and recruited from eleven primary-care practices in Ontario, Canada. Mean age was 38 ± 14 months; 124 children were girls (50 percent). The children received either a placebo syrup containing sorbitol or a xylitol syrup twice daily for six months. The primary endpoint was the number of physician-diagnosed otitis media episodes. Three episodes occurred in the placebo group of 125 children and six in the xylitol group of 125 children (OR 2.04; 95-percent confidence interval 0.43 to 12.92; p = 0.50). No difference was found in caregiver-reported upper-respiratory-tract infections (rate ratio 0.88; 95-percent confidence interval 0.70 to 1.11) or in caries (four children on sorbitol, two on xylitol; OR 0.42). The sorbitol syrup served as the placebo arm; xylitol was tested; the study says nothing about a preventive effect of sorbitol.

The 2025 work on regioselective glycosylation of an 18F-labelled sorbitol ¹³ belongs to imaging rather than therapy. It addresses whether the diagnostic properties of the sorbitol derivative [18F]-FDS can be improved by glycosylation with regard to stability, breadth of captured pathogens and body distribution. [18F]-FDG was chemoenzymatically converted into α - and β -linked disaccharides and reduced to the glycosylated derivatives [18F]-FNT (α -1,3), [18F]-FMT (α -1,4), [18F]-FLT (β -1,3) and [18F]-FCT (β -1,4). The α -linked variants [18F]-FNT and [18F]-FMT were taken up more strongly by gram-positive and gram-negative pathogens than the β -linked variants. The work concerns a labelled sorbitol derivative, not sorbitol as an active substance; whether a clinically usable infection detection method results from this remains open.

Safety and Tolerability

The open-label phase-I study from 2024 ²⁷ compared a new paediatric formulation of paracetamol with an already marketed one. Both contain 24 mg paracetamol per millilitre; the new formulation has a finer active-substance particle size and lower amounts of maltitol (5.85 g per dose versus 7.25 g) and sorbitol (2.4 g per dose versus 2.83 g). AUC_{0-tlast}, C_{max} and t_{max} were recorded; median t_{max} was 1.00 hour in both groups and mean C_{max} values were comparable. Participants were 42.9 percent female and 57.1 percent male; median age was 30 years. Because sorbitol content, maltitol content and particle size changed simultaneously, tolerability of the sorbitol amount cannot be evaluated separately from this work.

The open, randomised phase-I study from 2025 ²⁸ determined the bioavailability of three intranasal formulations of azelastine hydrochloride in healthy male volunteers: two new formulations containing 0.10 percent and 0.15 percent azelastine with sorbitol and sucralose, and a marketed 0.10-percent formulation. 54 subjects were allocated to the three treatments. Maximum plasma concentration and area under the concentration-time curve were similar for azelastine and its metabolite desmethylazelastine with treatments A and C (0.10 percent). The most frequent adverse events were rhinorrhoea (5.6 percent) and sneezing (5.6 percent). Sorbitol is an excipient here; the study examines azelastine uptake and not the effect or tolerability of sorbitol.

Gut and Microbiome

The prospective, randomised 2025 study at five Korean tertiary-care clinics ² compared two bowel preparations before colonoscopy: 0.46 L of a solution of D-sorbitol, ascorbic acid and picosulfate given on the same day or 2 L of polyethylene glycol with ascorbic acid in split dosing. 243 patients were enrolled (mean age 50.6 years; 39.6 percent male); 122 received the sorbitol combination. Cleansing was assessed with the Harefield Cleansing Scale by independent, blinded raters. The proportion of successful cleansings was similar (96.8 percent versus 96.7 percent; p = 1.000); clinical and laboratory safety parameters did not differ. Significantly fewer patients found intake difficult (22.1 percent versus 81.0 percent; p < 0.01) and satisfaction was higher (8.71 versus 6.22; p < 0.001). The effect of sorbitol alone cannot be derived from a triple combination.

The 2023 work on targeted analysis of gut-microbiome metabolites ¹² examined serum and urine from 20 healthy individuals and 90 patients with type-2 diabetes and diabetic kidney disease at various stages (normoalbuminuria with uACR below 30 mg/g, microalbuminuria 30–300 mg/g, macroalbuminuria above 300 mg/g). Quantification used reference standards as well as limits of detection and quantification. Potential biomarkers of early diabetic kidney

disease identified in serum were arginine, dimethylarginine, hippuric acid, indoxyl sulphate, butenylcarnitine and sorbitol; in urine p-cresyl sulphate. The work describes an association between a measured value and disease stage; whether sorbitol is cause, consequence or concomitant feature cannot be decided from a cross-sectional comparison.

The 2023 review ³⁰ describes how *Clostridioides difficile* survives in the gut and causes disease. Antibiotic administration is regarded as the most important risk factor because a disturbed gut flora permits colonisation; colonisation resistance also arises through nutrient competition. *C. difficile* can utilise carbon dioxide, the amino acids proline, hydroxyproline and ornithine, the membrane component ethanolamine and the carbohydrates trehalose, cellobiose, sorbitol and mucin degradation products as carbon and energy sources. Zinc binding by the host response alters the pathogen's metabolism and could indicate an inflamed gut milieu in which abundant nutrients are available. The metabolite p-cresol inhibits growth of commensal species and thereby promotes dysbiosis. Sorbitol appears here as a nutrient of the pathogen; whether a sorbitol-poor diet influences the course has not been tested.

Musculoskeletal System

The cross-sectional multicentre study from 2025 ⁹ recorded 144 patients from 126 families with biallelic loss-of-function mutations in the sorbitol dehydrogenase gene *SORD*, including 99 men (69 percent) and 45 women (31 percent) of European, Hispanic, Chinese, Middle-Eastern and North-African ancestry. The most frequent disease-causing variant was c.757delG (p.Ala253GlnfsTer27), followed by c.458C>A (p.Ala153Asp); further variants occurred predominantly in single cases. Two thirds of affected individuals had CMT2 and one third distal hereditary motor neuropathy; disease onset was usually in the second decade of life. Foot dorsiflexion was most severely affected, with dorsal and plantar flexion showing similar degrees of weakness.

The mean sorbitol concentration was significantly higher in CMT-SORD patients than in controls and heterozygous carriers, independent of serum storage duration, sex and variant type. A multicentre phase-2/3 study with the aldose reductase inhibitor Govorestat (NCT05397665) is currently underway. The cross-sectional survey thus shows that the disease can be captured genetically and biochemically; whether lowering the sorbitol concentration alters the course is being examined by the ongoing study.

Oxidative Stress

The work from 2026 ³² examined how the polyol pathway and aldehyde detoxification behave under metabolic and oxidative stress in the human neuroblastoma cell lines LAN-5 and SH-SY5Y. The cells were maintained in hyperglycaemic medium and additionally treated with 4-hydroxynonenal; protein expression and enzyme activities were measured. Under hyperglycaemia, the activity of aldose reductase AKR1B1 and sorbitol accumulation increased. Both cell lines exhibited an incomplete profile of HNE-detoxifying enzymes; ALDH1A1 and AKR1C3 were not formed. 4-Hydroxynonenal reduced cell viability in 2D and 3D models. Inhibition of AKR1B1, but not of CBR1, enhanced the cytotoxicity induced by 4-hydroxynonenal.

These findings derive from cell cultures, partly in 2D and 3D models, and are therefore preclinical; treatments with sorbinil or rutin during the stress phase were also examined. They show that sorbitol accumulates in neuroblastoma cells as a product of an activated polyol pathway and that aldose reductase is simultaneously involved in the detoxification of aldehydes. **Hypothesis:** If the polyol pathway is inhibited, the aldehyde load in tumour cells could increase. Whether this yields a therapeutic target remains open.

Overall Picture

Across the areas, one feature stands out: in most of these works sorbitol does not appear as the test substance but as a comparator arm, excipient, nutrient or metabolic product. In oral health it serves as the control versus xylitol, ³¹ or as the unchanged comparator solution in the plaque-pH trial ⁵, in the paediatric otitis media study as the placebo syrup ²⁶, in the bioequivalence studies as an excipient ^{27, 28}, in microbiome research as a substrate of the pathogen ³⁰ and as a biomarker ¹², and in neuropathy and neuroblastoma as an accruing polyol ^{6, 9, 32}. Where sorbitol itself was tested, this occurred within narrowly defined questions: the bitterness of asenapine ^{7, 3}, preparation before colonoscopy ² and lifelong avoidance in hereditary fructose intolerance.

The strength of evidence differs markedly across areas. Systematic reviews and larger controlled studies exist for oral health, ³¹ bowel preparation ² and otitis media ²⁶; the weight-loss study ¹ examined erythritol, not sorbitol. The findings on CMT-SORD ⁹, metabolism in PMM2-CDG ¹¹, neuroblastoma ³² and tracer development ¹³ are preclinical. Open questions concern the separation of components in combination products, clinical endpoints rather than surrogate measures, and whether the measured sorbitol concentrations can be specifically modulated.

Methodology of the Evidence Base

The works range from systematic reviews, ^{31, 10, 6, 30} through randomised controlled crossover and parallel-group studies ^{7, 26, 2, 4, 8, 5, 27, 28, 3, 1} and observational or cross-sectional surveys, ^{12, 9} to cell-culture, animal and tracer studies ^{11, 13, 32}. Observation periods range from six months in the paediatric study ²⁶, two years in the weight-loss study ¹, six hours in the exposure chamber ⁸ and 30 minutes for plaque-pH measurement ⁵; bioequivalence studies use single doses and short wash-out phases ²⁷. Target variables include gingival and plaque indices, taste and satisfaction questionnaires, plasma concentrations and cleansing scales. Studies in which sorbitol itself constitutes the tested intake with a clinical endpoint, and investigations that compare the individual components of combination products head-to-head, are systematically absent.

The Most-Cited Works Do Not Concern Sorbitol

The thesis can be read from the titles. The most-cited controlled work in the field examines sugar-free polyol chewing gums and gingival inflammation; the second most-cited examines pretreatment with D-sorbitol against the bitterness of asenapine — the taste perception of the other active substance is tested there. Further highly cited human studies address the bioequivalence of epalrestat, a paracetamol-containing paediatric suspension, an azelastine nasal spray and xylitol in acute otitis media. Sorbitol as an independent test substance is the exception.

This is not a shortcoming of the works — they cleanly investigate what they set out to examine. It is a question of attribution: anyone who reads citation counts as weight for sorbitol is counting works in which the substance is merely carried along. Conversely, the independent sorbitol investigations lie where combinations are tested — a bowel-cleansing solution of three components, a nasal spray of carrageenan and sorbitol.

PLAUSIBLE:

From such mixture studies the effect of the single substance cannot be calculated. The result is a literature with many points of contact and few investigations in which sorbitol alone is tested.

3. How Robust the Research Is

The human literature is distributed across controlled and observational works. The human studies examine primarily **safety** (5 works) and **bioavailability** (4); thereafter follow **metabolism** and **gut** with three works each, **immune system** and **antiviral** questions with two each, and one work each on **cardiovascular** and **inflammation**. No therapeutic leading area emerges. The clearest trace is dental: the most-cited work is a systematic review on sugar-free polyol chewing gums and gingival inflammation. In a controlled study on xylitol in acute otitis media, sorbitol was a component of the placebo syrup.

Methodologically the field stands on solid ground at several points: randomised, single-blind, placebo-controlled crossover studies, a prospective, multicentre, randomised trial of a bowel-cleansing solution, systematic reviews. Such designs reliably address **safety**, **tolerability** and **bioequivalence** questions. What they do not support is a statement about the effect of sorbitol itself: where the substance is merely a formulation component, no contribution of the single substance can be derived from the result. **Hypothesis:** Part of the high citation counts is explained precisely by the fact that sorbitol is carried along in these works as a formulation component and is not treated as the investigational subject. The most highly cited works in the collection are basic-science studies on microbial and foetal metabolism.

4. What Is Frequently Claimed — and What the Data Support

STATEMENT	EVIDENCE BASE
Sorbitol lowers blood glucose	There is also a review on sugar substitutes as an antidiabetic adjunct, conducted as an observational study. The collection does not contain a controlled test of
Sorbitol acts against caries	The most frequently cited controlled study examines sugar-free polyol chewing gums as a whole, not sorbitol. The biofilm model shows an inhibition of Strept
Sorbitol has a decongestant effect in allergic rhinitis	A nasal spray consisting of carrageenan and sorbitol was tested against a saline solution in seasonal allergic rhinitis. No contribution of the individual compone
Sorbitol cleanses the bowel before colonoscopy	A solution consisting of D-sorbitol, ascorbic acid and picosulfate was investigated in a prospective, multicentre, randomised study. Zur Wirkung von Sorbitol al

5. Profile: Molecule and Charge

Sorbitol is not a single molecule but a **mixture** — there is no molecular formula and no fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; that is exactly what the next section addresses.

6. Charge, Electrons, Radicals

Sorbitol does not appear in the present works as an independent redox or charge system. In one cell-culture study, assays showed radical-scavenging capacity as well as inhibitory activity against selected pathogenic bacterial and fungal strains ¹⁷; whether sorbitol itself was the active constituent is not apparent from the sentence. In an animal study, high removal efficiency was attributed to synergistic mechanisms, including electrostatic interactions, hydrogen bonds, π - π stacking and iron chelation ¹⁸. Sorbitol is not named there as the carrier of these mechanisms. A basic-science paper describes sorbitol merely as a polyvalent compound in ethanol-based fixative solutions alongside polyethylene glycol and chelators ¹⁹. A further basic-science paper deals with protein-ligand interactions and the nature of molecular recognition, without naming sorbitol.

A foundational study utilises the property that the nitrogen-containing quaternary ammonium group in the ChCl molecule can form free radicals under UV irradiation to polymerise acrylamide without an initiator; sorbitol is not involved. In an agricultural context, the sorbitol metabolism was investigated in *S. cerevisiae* strains that functionally express heterologous genes for RuBisCO and PRK to enable the re-oxidation of additional NADH through alcoholic

fermentation ²⁰. Further agricultural studies concern exogenous, sorbitol-chelated calcium: It alleviates cadmium toxicity in peanut seedlings via physiological, biochemical and transcriptomic regulation ²¹, whereby a controlled comparison was carried out on peanut seedlings under Cd stress with inorganic calcium or sorbitol-chelated calcium at the same calcium concentration ²¹. The inhibition led to a marked accumulation of reactive oxygen species in the plants ²¹. In humans, these evidence sentences contain no electrochemical measurement of sorbitol. It would need to be clarified whether the charge state, radical formation or electron transfer of sorbitol in human samples can be measured at all and which method would be suitable for this.

7. Interactions with Other Substances

With which other substances of the platform this substance is **jointly** investigated or discussed in human studies and review articles — combination, comparison or common mechanism of action. The number indicates studies in which both occur.

SUBSTANCE	JOINT STUDIES	OF WHICH CONTROLLED IN HUMANS
Acceptance and Commitment Therapy (ACT)	10	2
Chronic Inflammation	4	1
Stress, Cortisol and Inflammation	4	0
Art Therapy	4	1
S-Adenosylmethionine (SAME)	4	3
Gut Microbiome	3	0
Low-FODMAP Diet	3	2
Vitamin C	3	1
Blood Flow Restriction Training (BFR)	2	0
Hyaluronic Acid (oral)	2	0

In humans, a controlled study examined the bioavailability of two new intranasal azelastine formulations (0.10 % and 0.15 %) containing sorbitol and sucralose against the commercially available 0.10 % azelastine (.). This investigated the influence of the additive on the uptake of a medicinal substance via the nasal mucosa; the sentences do not indicate whether sorbitol itself alters uptake. In an observation in humans, sorbitol was part of a metabolite panel consisting of 4-dodecylbenzenesulfonic acid, carnosol and sorbitol that, together with clinical signs and nPCR, can aid differentiation between HSK and BKC (²²).

In cell culture, the combination of D-sorbitol and xylitol had a higher genotoxic potential than D-sorbitol alone, due to additive or synergistic interactions between food additives (²³, ²³). In *Komagataella phaffii*, sorbitol acts as a non-repressive carbon source together with formate, which induces the AOX1 promoter (²⁴). With soya oil, sorbitol acted synergistically in shake flasks and maximised lipase production (13.56 U mL⁻¹); in the stirred-tank bioreactor, however, it strongly inhibited enzyme expression (²⁵). It would need to be clarified whether sorbitol alters CYP enzymes or the plasma protein binding of medicinal substances.

8. Overdose, Tolerability, Limits

Limited data from controlled studies are available on adverse effects of sorbitol-containing preparations in humans. In a randomised, single-blind crossover study, D-sorbitol was investigated as a single dose prior to sublingual administration of asenapine; the background was the bitter taste that frequently leads to discontinuation of medication ⁷. The work thus describes an application problem, not the tolerability of sorbitol itself. In a prospective, multicentre, randomised study on bowel cleansing with a solution of D-sorbitol, ascorbic acid and picosulfate, 243 patients were enrolled, 122 of whom received the tested preparation ². The most frequent adverse events were rhinorrhoea and sneezing at 5.6 % each ²⁸. Intake was described as difficult by 22.1 % versus 81.0 %, and satisfaction was 8.71 versus 6.22 ².

An upper limit or dose-related toxicity of sorbitol cannot be derived from these findings. The figures cited refer to a combination solution, not the single substance, and therefore permit no statement about sorbitol alone. In an observational study of 86 participants, an injectable preparation of 2.6 % high-molecular-weight hyaluronic acid and 3.2 % sorbitol was investigated for improving skin biomechanics ²⁹; here too, the safety assessment concerns the mixture. For the other cited controlled studies on xylitol, paracetamol, epalrestat and asenapine, no adverse effects of sorbitol are reported ²⁶ ²⁷. It would need to be examined which doses of sorbitol alone, by which routes of administration, trigger gastrointestinal or other events and how these can be separated from the accompanying substances of the investigated solutions.

9. The Most Robust Studies

Ordered by strength of evidence, not by familiarity: review articles and studies with many participants first. The complete evaluation comprises considerably more studies; the most robust ones are listed here.

Controlled Studies in Humans

- Effects of sugar-free polyol chewing gums on gingival inflammation: a systematic review (2022) — Review article
- ¹ Declines in Plasma Erythritol and Improvements in Cardiovascular Risk and Atherogenic Lipid Profiles: A 2-Year Randomized Weight-Loss Dietary ... (2026) — 802 participants
- ² Efficacy and safety of a New D-sorbitol, Ascorbic Acid, and Picosulfate Bowel Cleansing Solution for colonoscopy: A prospective, multicenter ... (2025) — 243 participants
- ³ Sensory evaluation of the bitterness of asenapine using D-sorbitol pretreatment: single-blind, placebo-controlled, crossover trial (2023) — 20 participants
- ⁴ Decongestant Effect of "Coldamaris Akut", a Carrageenan- and Sorbitol-Containing Nasal Spray in Seasonal Allergic Rhinitis (2024)
- ⁵ Clinical Evaluation of the Effect of Nanohydroxyapatite Lozenge on the pH of Dental Plaque (2024)
- Bioequivalence Study of Epalrestat for Healthy Chinese Subjects (2024)
- Xylitol for the prevention of acute otitis media episodes in children aged 1-5 years: a randomised controlled trial (2024) — 59 participants
- Bioequivalence of a New Pediatric Paracetamol Oral Suspension Compared With a Marketed Formulation in Healthy Adults: A Randomized, Open-Label Study (2024)
- ⁶ Chronic idiopathic axonal neuropathy: antibodies, genetics, and beyond (2025)
- ⁷ Effect of single-administration of D-sorbitol pretreatment on the bitterness and continued willingness to take asenapine: a randomized, single-blind ... (2024)
- ⁸ Demonstration of a Decongestant Effect of "Coldamaris Akut" Compared to Saline Nasal Spray in Participants Suffering from Seasonal Allergic Rhinitis (2024) — 46 participants
- Determination of the Bioavailability of 3 Intranasal Formulations of Azelastine Hydrochloride in Healthy Male Volunteers (2025) — 54 participants

Observational Studies in Humans

- ⁹ Genotype and phenotype spectrum of Charcot-Marie-Tooth disease due to mutations in SORD (2025) — 144 participants
- ¹⁰ Suitability of sugar alcohols as antidiabetic supplements: A review (2021)
- ¹¹ Tracer metabolomics reveals the role of aldose reductase in glycosylation (2023)
- ¹² Quantitative, Targeted Analysis of Gut Microbiota Derived Metabolites Provides Novel Biomarkers of Early Diabetic Kidney Disease in Type 2 Diabetes ... (2023)
- Vitamin C and folate status in hereditary fructose intolerance (2022)
- ¹³ Regioselective Glycosylation of Fluorine-18-Labeled Sorbitol for Enhanced Bacterial Detection In Vivo Using PET (2025)
- Is the Rate of Responders to Hyaluronic Acid Injection for Patients with Knee Osteoarthritis Stable Over Time? Post hoc Analyses of a 6-Month ... (2023) — 96 participants
- ¹⁴ Current Dietary Practices in Hereditary Fructose Intolerance: Results from a National Survey Across 15 Italian Metabolic Centres (2026)
- ¹⁵ TIGAR coordinates polyol and glutamine metabolism to regulate CD4+ T cells (2026)
- Effects of L-Ornithine-L-Aspartate on Angiogenesis and Perfusion in Subacute Hind Limb Ischemia: Preliminary Study (2024)
- ¹⁶ Descriptive Analysis of Carrier and Affected Hereditary Fructose Intolerance in Women during Pregnancy (2024)

10. Summary

The controlled human studies include randomised, single-blind, placebo-controlled crossover studies on safety, tolerability and bioequivalence issues as well as a prospective, multicentre, randomised examination of a bowel cleansing solution; observational studies and systematic reviews are also included. The human studies are distributed across safety (5 studies), bioavailability (4), metabolism and gut (3 each), immune system and antiviral questions (2 each) and one study each on cardiovascular and inflammation. No therapeutic focus area is emerging. The clearest trace is a dental one; the most cited review on sugar-free polyol chewing gums bases its sorbitol statement on a single included study.

From combination products such as the carrageenan- and sorbitol-containing nasal spray, no effect of sorbitol alone can be derived; what role it plays would need to be clarified with a design that compares the components individually. In hereditary fructose intolerance, sorbitol appears as a component of the diet to be avoided, not as a test substance.

A sufficiently large study on sorbitol-sweetened chewing gums with standardised chewing time, intake amount and a gingival index as the primary endpoint would clarify the open question of the 2022 review. Whether the lower bitterness of asenapine actually leads to better treatment adherence also remains open; both endpoints of the crossover study are questionnaires. The 2021 metabolism review lacks a uniform clinical endpoint, and the tolerable amount has not been conclusively clarified. In SORD-related sorbitol accumulation, it is open which patients would clinically benefit from a reduction.

11. What Remains Open

- **Comparison group:** Whether sorbitol without further formulation components has measurable effects in humans has not been tested in isolation in any controlled study of the collection.

- **Caries prevention:** Whether the sugar alcohol itself has a caries-preventive effect or merely replaces sugar cannot be separated from the reviews on polyol chewing gums.
- **Polyol pathway:** The pathway from glucose via sorbitol to fructose is described in several works; whether this results in a therapeutic target remains open.

12. Further Paths

Topics, mechanisms of action and chains in which this substance occurs — for all those who want to look beyond the substance.

- Interaction network

Frequently Asked Questions

Is Sorbitol an active substance or an excipient in these studies?

In the human studies available, it is predominantly a component of the formulation. It appears as a sugar alcohol in chewing gums, as an additive in nasal sprays and lozenges, and as one of three components of a bowel-cleansing solution. As an independent test substance it occurs in the controlled studies only in the pretreatment for bitterness modulation.

What does dental research contribute?

The dental research line is the strongest in the field. The most frequently cited controlled work is a systematic review on sugar-free polyol chewing gums and gingival inflammation. A laboratory model shows that xylitol and sorbitol inhibit biofilms of *Streptococcus mutans* and *Candida albicans* and that sucrose attenuates this effect. Both are indications, not a test of sorbitol in humans.

Are children represented in the studies?

Yes, in individual studies. A randomised controlled trial examines xylitol in acute otitis media in children aged 1 to 5 years; it concerns xylitol, not sorbitol. A bioequivalence study on a paracetamol-containing paediatric suspension, by contrast, was conducted in healthy adults.

Sources

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Unger-Manhart N, Morokutti-Kurz M, Zieglmayer P, Russo A, Siegl C, König-Schuster M et al. · 2024
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- In vitro assays demonstrate radical scavenging capacity and inhibitory activity against selected pathogenic bacterial an...
· 2026
- The high removal efficiency was attributed to synergistic mechanisms, including electrostatic interactions, hydrogen bon...
· 2026
- This study aimed to develop an optimized ethanol-based fixative to preserve DNA and RNA in cervical samples under ambien...
· 2026
- To enable re-oxidation of this additional NADH by alcoholic fermentation, sorbitol metabolism was studied in *S. cerevisi*...
· 2022
- Exogenous sorbitol-chelated calcium mitigates toxicity of cadmium in peanut seedlings through physiological, biochemical...
· 2026
- The combination of clinical signs with nPCR result and a metabolite panel (4-Dodecylbenzenesulfonic Acid+ Carnosol +Sorb...
· 2026
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· 2026
- In *Komagataella phaffii*, the use of formate as an AOX1 promoter (PAOX1) inducer in combination with sorbitol,...
· 2025
- Here we show that while sorbitol acts synergistically with soybean oil to maximize lipase production in shake flasks (13...
· 2026
- The most common adverse event was diarrhoea (28% with placebo; 34% with xylitol). Conclusions Regular use of xyli...
· 2024
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· 2024
- The most frequently reported adverse events were rhinorrhea (5.6%) and sneezing (5.6%)....
· 2025
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Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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