Review

No benefit of soluble fiber on liver function

Editor's Choice

A systematic review and meta-analysis of controlled trials

Abed Ghavami[1], Sepide Talebi[2], Hanieh Barghchi[3], Elyas Nattagh-Eshtivani[4], Hamed Mohammadi[2], and Rahele Ziaei[5]

[1] Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Iran
[2] Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Iran
[3] Department of Nutrition, Faculty of Medicine, Mashhad University of Medical Sciences, Iran
[4] Nutrition, Food Sciences and Clinical Biochemistry Department, School of Medicine, Social Development and Health Promotion Research Center, Gonabad University of Medical Sciences, Iran
[5] Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Iran

Abstract: *Background:* To conduct a systematic review and dose-response meta-analysis of current findings from randomized controlled trials (RCTs) on the effect of soluble fiber supplementation on liver function in both healthy individuals and people with specific health conditions, PubMed, Scopus, and ISI Web of Science were systematically searched for relevant RCTs published prior to April 2022. *Methods:* We estimated the change in liver function parameters for each 5 g/d increment in soluble fiber in each trial and then calculated the mean difference (MD) and 95%CI. A total of 25 RCTs with 27 treatment arms (1744 subjects; 884 cases, 860 controls) were included. *Results:* A total of 25 RCTs with 27 treatment arms were included. The intervention duration of the included studies ranged from 3 to 52 weeks and the dose of soluble fiber supplementation varied from 0.0025 to 40 g/d. Soluble fiber supplementation could not significantly affect serum alanine transaminase (MD: −0.02 U/L, 95% CI: −1.06 to 1.01), aspartate transaminase (MD: −0.34 U/L, 95% CI: −0.84 to 0.15), alkaline phosphatase (MD: 0.29 U/L, −0.14 to 0.71), gamma-glutamyl transferase (MD: 0.12 U/L; 95% CI: −0.81 to 1.05), serum bilirubin (MD: 0.42μmol/L, 95% CI: −0.08 to 0.93) and albumin (MD: 0.64 g/dl, 95% CI: −0.42 to 1.70) levels. *Conclusions:* Findings from this study did not support the beneficial effects of soluble fiber supplementation on liver function biomarkers. There is a need for long-term high-quality interventions to examine the effects of different types and doses of soluble fibers on liver function as primary outcome.

Keywords: soluble fiber, liver function test, meta-analysis

Introduction

Liver diseases are significant public health problems including alcoholic liver disease, non-alcoholic liver disease from steatosis to cirrhosis, acute and chronic viral hepatitis and hepatocellular carcinoma [1]. Metabolic syndrome, alcohol abuse, viruses, drugs and toxins are the main etiologies of liver diseases [1, 2]. The prevalence of hepatic disorders is increasing, as they account for 3.5% of all deaths around word, of which a half are due to the complications of cirrhosis with others being related to viral hepatitis and hepatocellular carcinoma [3]. Due to the growing trend of liver disease complications and mortality rate, proper prevention and management approaches can increase patients' quality of life and also improve public health [4].

Liver function test (LFT) biomarkers, which include alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and serum bilirubin (BIL) are useful diagnostic tools for hepatic disorders, such as non-alcoholic fatty liver disease (NAFLD) [5]. Inflammation, oxidative stress, lipid peroxidation and immune response disruption are major pathological processes involved in liver diseases [2, 6]. It has been proposed that dietary fibers beneficially affect oxidative stress and inflammatory responses, as their intake was associated with a reduced risk of type 2 diabetes (T2D) [7], hypertension [8] and cardiovascular diseases [9] in previous studies. The American Diabetes Association (ADA) recommends that dietary fiber intake in the general population should be about 14 g dietary fiber per 1,000 kcal [10]. However, since dietary fiber intake is much lower than dietary recommendations, supplementation with isolated or synthetic fibers has been suggested [11]. Physicochemical properties of dietary fibers such as their solubility, fermentability and viscosity determine their therapeutic effects. Soluble fiber intake has been associated with favorable effects on metabolic disorders [12, 13]. Several mechanisms have been proposed in this regard, among which the

https://doi.org/10.1024/0300-9831/a000800

beneficial effect of soluble fibers on gut microbiota and increased production of short-chain fatty acids (SCFA) should be highlighted [14].

Many randomized controlled trials (RCT) examining the effect of soluble dietary fiber supplementation on blood glucose and lipid control in healthy or obese individuals as well as subjects with diabetes, hypercholesterolemia, hyperuricemia or NAFLD, also report results for LFTs; however, their findings for LFTs were inconsistent despite similar methodology [15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41].

Considering the link between cardiometabolic risk factors and NAFLD, and the potential role of soluble fiber in improving blood glucose and lipid control, we aimed to conduct a systematic review and dose-response meta-analysis of current findings from RCTs to clarify the effect of soluble fiber supplementation on LFTs.

Methods

The protocol of this systematic review has been registered on PROSPERO website (https://www.crd.york.ac.uk/PROSPERO) (Registration ID: CRD42022338647) and developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [42].

Two authors (E.N.E. and H.B.) searched the following electronic database up to April 2022, with no restriction in date or language: PubMed, Scopus, and Web of Science and a manual search of RCT reference lists augmented database searches. Search strategy characteristics are outlined in the electronic supplementary material (ESM) 1, Table E1.

All clinical trials with either cross-over or parallel design which had at least two arms and investigated the effect of soluble fiber supplementation on one or more LFT markers such as ALT, AST, ALP, GGT, BIL or albumin (ALB) for more than two weeks compared to a control group were included in the present systematic review. Studies could be open-label or single-, double- or triple- blinded randomized trials. Studies were excluded if they were performed on pregnant or, lactating women, children or adolescents (<18 years old), if they implemented soluble fiber in combination with another substance, if they did not report mean and standard deviation (SD) for at least one LFT, if they did not have a control group, or if they were reported in the grey literature such as conference papers, dissertations, and patents.

Two authors (R.Z., A.G.) extracted the data independently. Any discrepancies were resolved by consensus between the two authors and a third author made a final decision if this was not possible. Data extracted from eligible studies included first author's family name, country and publication year, participants' characteristics such as age, gender, population and mean BMI, sample size, study characteristics such as design, duration, blinding, type, dose and form of administration of soluble fiber supplements, and final investigated markers.

Quality assessment was undertaken to assess the rigor of RCTs as determined by the risk of bias utilizing the Cochrane Risk of Bias Assessment Tool (38). Evaluation of RCT quality (bias) was based on seven domains: participant randomization sequence generation, supplement allocation concealment, blinding of participants and research personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias sources. The risk of bias for each study was then rated as low (adequate information provided), unclear (if certain information was unclear or indeterminate), and high (if there was a serious concern in the criteria). The overall quality of RCTs was subsequently categorized, similar to prior established methodology, as low if all domains were determined to have a low risk of bias, high if at least one domain was at high risk of bias, or unclear if at least one domain had an unclear risk of bias yet no domain had high risk.

The Grading of Recommendations Assessment, Development and Evaluation (39) method was considered to evaluate the certainty of the evidence for outcomes. The quality of the assessed evidence was rated as high, moderate, low, and very low. High grades suggest high confidence that the actual effect is commensurate with the estimated effect. Moderate grades suggest that the actual effect is likely to be close to the estimate of the effect; however, there exists a small possibility of substantial differences. A low grade suggests a greater likelihood that the true effect may be substantially different from the estimate of the effect, and very low grades suggest the true effect is likely different from the estimated effect (40). Further, RCTs with an initial high quality of evidence evaluation may be downgraded based on study limitations, including risk of bias inconsistency (substantial unexplained heterogeneity, $I^2>50\%$; $p<0.05$) and imprecision (95% CI for effect estimates are wide or cross the minimally significant threshold difference for clinical benefit). Minimal thresholds for clinically important changes and consider indirectness of outcomes (primary outcomes presented are surrogate rather than patient-important outcomes (41) and other considerations (publication bias and dose-response gradient usage.

Data from included studies were analyzed using mean difference with standard deviation (SD). The random-effects model was applied to compute Weighted Mean Differences (WMDs) with 95% Confidence Intervals (CIs) for all selected indices. The following formula was used to calculate SD: SD=SEM$\times$square root of n (n; the number of subjects) [43] when only the Standard Error of Mean (SEM) was available. When the outcome measures were reported in median and range (or 95% CI), mean and SD values were calculated by Hozo et al. [44] method. For assessing between-study heterogeneity, I-square (I^2) test and subgroup analysis were employed. Based on the following variables, subgroup analysis was conducted to find the source of heterogeneity: gender (male, female and both), study duration (≤8 vs. >8 weeks), dose of soluble fiber supplement (≤10 vs. >10 g/day), baseline BMI (≥30 vs. <30 Kg/m^2) mean age (≥50 vs. <50 years), fermentability (fermented, non-fermented and mix), viscosity (viscous vs. non-viscous) and study population (healthy, steatohepatitis, overweight and obese, diabetes and other). Publication bias was assessed by Egger's regression and Begg's test [45]. Sensitivity analysis was utilized to check the accuracy of the final results [46]. The mean and corresponding SD of change in liver function test, along with the number of participants in each study arm, was used to conduct a random-effects model for each 5 g/d increase in soluble fiber supplementation in the intervention group on changes in LFT [47]. To explore the shape of the effect of different doses of soluble fiber on LFT, we conducted a dose-response meta-analysis [48]. STATA version 17 software (Stata Corp, College Station, Texas, USA) was used to determine differences between pre- to post-intervention and control arm values. All differences in outcomes data were considered statistically significant at P≤0.05.

Results

We identified 10150 publications through initial electronic searches. Of those 8708 were removed based on duplicates (n=74), animal or irrelevant studies (n=7902) and acute phase (n=294) or review (n=438) studies. In the next step, 1442 trials remained for screening of the title and abstract of which 1410 papers were excluded due to unrelated topics, book chapters, letters, conference reports and review articles. Then out of 33 articles which their full texts had been checked, 7 papers were excluded because of following reasons: insufficient data (n=4) [49, 50, 51, 52], no control group (n=1) [53], duplicated reports (n=1) [54] and pregnant women (n=1) [55]. Detailed reasons for study exclusion were described in ESM 1, Table E2. Ultimately, 25 studies met our inclusion criteria. Details of included studies extracted for analysis were shown in Table 1. The study selection process was shown in Figure 1. Sensitivity analyses utilizing a range of correlation coefficients between 0.25 and 0.75 were shown in ESM 1, Table E3.

The effect of the soluble fiber supplementation on ALT level was examined in 25 studies with 27 treatment arms containing 1744 subjects (884 cases, 860 control). The pooled analysis demonstrated that soluble fiber supplementation induced a non-significant decrease in ALT compared to the placebo group (MD: −0.02 U/L, 95% CI: −1.06 to 1.01, P=0.962), without any significant between-study heterogeneity (I^2=13.6%, P=0.263) Table 2. Additional analysis showed a greater reduction in ALT in trials with a longer duration (≥8 weeks) (MD: −0.93 U/L, 95% CI: −2.52 to 0.7, P=0.265), and in studies that supplemented soluble fiber with viscous characteristics (MD: −0.79 U/L, 95% CI: −2.82 to 1.25, P=0.448) ESM 1, Table E4.

Based on sensitivity analysis, no individual trial had a significant effect on the overall pooled effect size. There was no indication of publication bias using the Egger's test (P=0.122) or Begg's test (P=0.559).

A non-significant increase in ALT level by 0.33 (−0.10 to 0.76), P=0.130; (I^2=4.9%, P=0.392) following each 5 g/d increment in soluble fiber was seen Table 2. Moreover, dose-dependent analysis showed a non-significant proportional increase in ALT with the increase in soluble fiber consumption ($P_{dose\text{-}response}$=0.426 in a linear manner $P_{non\text{-}linearity}$=0.772) Figure 2 and ESM 1, Table E5.

The effect of soluble fiber supplementation on AST level was evaluated in 24 studies with 27 treatment arms, including a total of 2296 participants (1124 cases, 1172 control). AST had a non-significant reduction following soluble fiber supplementation compared to the control group (MD: −0.34 U/L, 95% CI: −0.84 to 0.15, P=0.177), without any significant between-study heterogeneity (I^2=0.0%, P=0.661) Table 2. Subgroup analysis also showed a greater reduction in people with steatohepatitis (MD: −3.23 U/L, 95% CI: −19.15 to 12.68, P=0.690) compared to other subgroups, and when soluble fiber was supplemented in long duration (MD: −0.58 U/L, 95% CI: −1.45 to 0.29, P=0.193) ESM 1, Table E4.

The overall pooled effect size was not affected by any individual studies based on sensitivity analysis. Furthermore, the Egger's test (P=0.428) or Begg's test (P=0.677) showed no significant publication bias.

Each 5 g/d increment in soluble fiber supplementation was associated with reduced AST level by −0.06 U/L (95%CI: −0.33, 0.21, P=0.673; (I^2=0.0%, P=0.549), based on linear dose-response meta-analyses Table 2. Soluble fiber had no significant dose-dependent effect on AST ($P_{dose\text{-}response}$=0.368, $P_{non\text{-}linearity}$=0.177) Figure 3 and ESM 1, Table E5.

The effect of soluble fiber supplementation on ALP concentrations was examined in 11 trials including 12 treatment arms, with 805 participants (414 cases, 391 control). We found that soluble fiber supplementation could not significantly affect ALP level compared to placebo (MD: 0.29 U/L, −0.14 to 0.71, P=0.181) and heterogeneity was not significant (I^2=0.0%, P=0.926) Table 2. Subgroup analysis

Table 1. Characteristics of eligible studies examining the effect of soluble fiber supplementation on liver function test

		Participants characteristic			Intervention/Control characteristic									
Study	Population	Gender (M/F)	Mean BMI (kg/m^2)	Mean age (y)	Location	Design	Duration (week)	Blinding	Soluble fiber	Dose (g/d)	Form of administration	Comparator	Background diet	Outcomes reported
Park et al. (2021) [68]	Habitual alcohol drinkers	M	27.5	48.9	Korea	P	12	D	Barley sprouts extract	0.48	Capsule	Maltodextrine	Usual	ALT, AST, GGT
Cicero et al. (2020) [17]	Moderate hypercholesterolemia	Both	NR	52.3	Italy	P	8	D	β-glucan from oat	3	Powder	Oat-based isocaloric placebo	A standardized diet	ALT, AST
Hiel et al. (2020) [29]	Obesity & at least one obesity-related metabolic disorder	Both	36.3	41.5	Belgium	P	12	S	Native inulin	16	Powder	Maltodextrine	Hypocaloric diet	ALT, AST, GGT
Reimer et al. (2020) [30]	Overweight/obese and T2DM	Both	39.9	54.8	Canada	P	52	D	PolyGlycopleX	15	Meal replacements	Rice flour	Hypocaloric diet	ALT, AST, ALP
Sakai et al. (2019) [25]	T2DM	Both	25.1	59.1	Japan	P	12	D	High molecular weight fucoidan	1.62	Beverage	Placebo beverage (starch)	Usual	ALT, AST, GGT,
Zhang et al. (2019) [31]	Normal-weight individuals	Both	21.0	36.5	China	P	4	D	high amylose resistant starch type 2	40	Powder	Starch	Diet based on chinese dietary guideline	AST, GGT
Evans et al. (2019) [19]	Healthy	Both	26.5	44.8	Canada	P	12	D	β-1,3-glucan from Euglena gracilis	0.36	Capsule	Microcrystalline cellulose	Usual	AST, BIL
Kitagawa et al. (2019) [23]	Healthy	Both	26.2	42.5	Japan	P	12	D	Resistant maltodextrin	5	Tea beverage	Tea beverage without RMD	Usual	AST, ALP, GGT, BIL, Alb
Lundby Hess et al. (2019) [32]	Overweight/obese	Both	33.7	48.6	Denmark	P	12	D	Resistant maltodextrin plus inulin	20	Semi-skimmed milk	Maltodextrine	Calorie-restricted diet	AST
Roshanravan et al. (2018) [69]	T2DM	Both	30.5	51.5	Iran	P	6	D	High-performance inulin	10	Powder	Starch	Usual	ALT, AST
Bomhof et al. (2018)-A [16]	NASH	Both	33.8	49.3	Canada	P	12	No	Oligofructose	8	Powder	Maltodextrine	Usual	ALT, ALP, GGT
Bomhof et al. (2018)-B [16]	NASH	Both	33.8	49.3	Canada	P	24	No	Oigofructose	16	Powder	Maltodextrine	Usual	ALT, ALP, GGT
Tayebi Khosroshahi et al. (2018) [27]	Hemodialysis patients	Both	23.4	56.0	Iran	P	25	D	High amylose resistant starch	8	Biscuit	Wheat flour	Usual	ALP, Alb
Buddington et al. (2017) [34]	Healthy adults with constipation	Both	29.0	33.3	USA	P	12	D	Oigofructose	15	Powder	Maltodextrine	Usual	ALT, AST, ALP, GGT, BIL
Gonai et al. (2017) [21]	T2DM	Both	28.0	50	Japan	P	4	No	Galacto-oligosaccharides	10	Syrup	Maltodextrine	Usual	ALT, AST
Lee et al. (2017) [24]	Healthy	Both	23.3	32.1	Korea	P	8	D	β-1,3-glucan	0.35	Capsule	Cellulose	Usual	ALT, AST
Akbarzadeh et al. (2016) [70]	Overweight/obese and NAFLD	Both	30.2	44.9	Iran	P	10	D	Psyllium	10	Powder	Ground wheat	Weight loss diet	ALT, AST

(Continued on next page)

Table 1. (Continued)

		Participants characteristic			Intervention/Control characteristic									
Study	Population	Gender (M/F)	Mean BMI (kg/m^2)	Mean age (y)	Location	Design	Duration (week)	Blinding	Soluble fiber	Dose (g/d)	Form of administration	Comparator	Background diet	Outcomes reported
Amar et al. (2016) [15]	Healthy	Both	25.0	34.0	USA	P	13	D	α-cyclodextrin	6	Tablet	Cellulose	Usual	ALT, AST, ALP, Alb
Mosikanon et al. (2016) [36]	Overweight/obese	Both	27.6	41.2	Thailand	P	6	D	β-glucan from yeast	0.47	Capsule	Rice flour	Usual	ALT, AST, ALP
Shimada et al. (2015) [26]	Hemodialysis patients	Both	22.1	66.8	Japan	P	8	T	polydextrose	10	Jelly	Placebo jelly	Usual	ALT, AST, GGT, Alb
Abbasalizad Farhangi et al. (2015) [20]	T2DM	F	29.1	48.3	Iran	P	8	D	oligofructose-enriched inulin	10	Powder	Maltodextrine	Usual	ALT, AST, ALP
Chang et al. (2013) [37]	Overweight/obese	Both	29.3	38.5	Taiwan	P	12	D	β-glucan from oat	1.5	Cereal	Cereal without beta-glucan	Usual	ALT, AST
Gaullier et al. (2011) [71]	Healthy elderly	Both	24.6	71.0	Norway	P	6	D	β-glucan from L. edodes mycelium	0.025	Tablet	Cellulose	Usual	ALT, AST, GGT, BIL
Hokazono et al. (2010) [22]	Mild hyperuricemia	Both	25.2	43.4	Japan	P	12	D	Fermented barley extract P	2	Drink	Placebo drink	Usual	ALT, AST, ALP, GGT, BIL, Alb
Wolever et al. (2010) – A [39]	Mild hyperuricemia	Both	27.4	52.0	Canada	P	4	D	High -MW beta-glucan from oat	3	Cereal	Wheat fiber	Usual	AST
Wolever et al. (2010) –B [39]	Mild hyperuricemia	Both	27.4	52.0	Canada	P	4	D	Medium-MW beta-glucan from oat	4	Cereal	Wheat fiber	Usual	AST
Wolever et al. (2010) – C [39]	Mild hyperuricemia	Both	27.4	52.0	Canada	P	4	D	Medium-MW beta-glucan from oat	3	Cereal	Wheat fiber	Usual	AST
Wolever et al. (2010) – D [39]	Mild hyperuricemia	Both	27.4	52.0	Canada	P	4	D	Low-MW beta-glucan from oat	4	Cereal	Wheat fiber	Usual	AST
Cloetens et al. (2009) [40]	Healthy	Both	20.9	24.0	Belgium	P	3	No	Arabinoxylan-oligosaccharides	10	Orange juice	Maltodextrine	Usual	ALT, AST, ALP, GGT, BIL, Alb
Carabin et al. (2009) [41]	Healthy	Both	31.6	22.7	Canada	P		D	PolyGlycopleX	-	Cereal	Skim milk powder	Usual	GGT
Daubioul et al. (2005) [18]	NASH	M	29.1	54.5	Belgium	P	8	D	oligofructose	16	Powder	Maltodextrine	Usual	ALT, AST, ALP, GGT, BIL

Abbreviations: M: male; F: female; T: triple; D: double; S: single; T2DM: type 2 diabetes mellitus; NASH: non-alcoholic steatohepatitis; NAFLD: non-alcoholic fatty liver disease; P: parallel; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; BIL: bilirubin; Alb: albumin; MW: molecular-weight; NR: not reported.

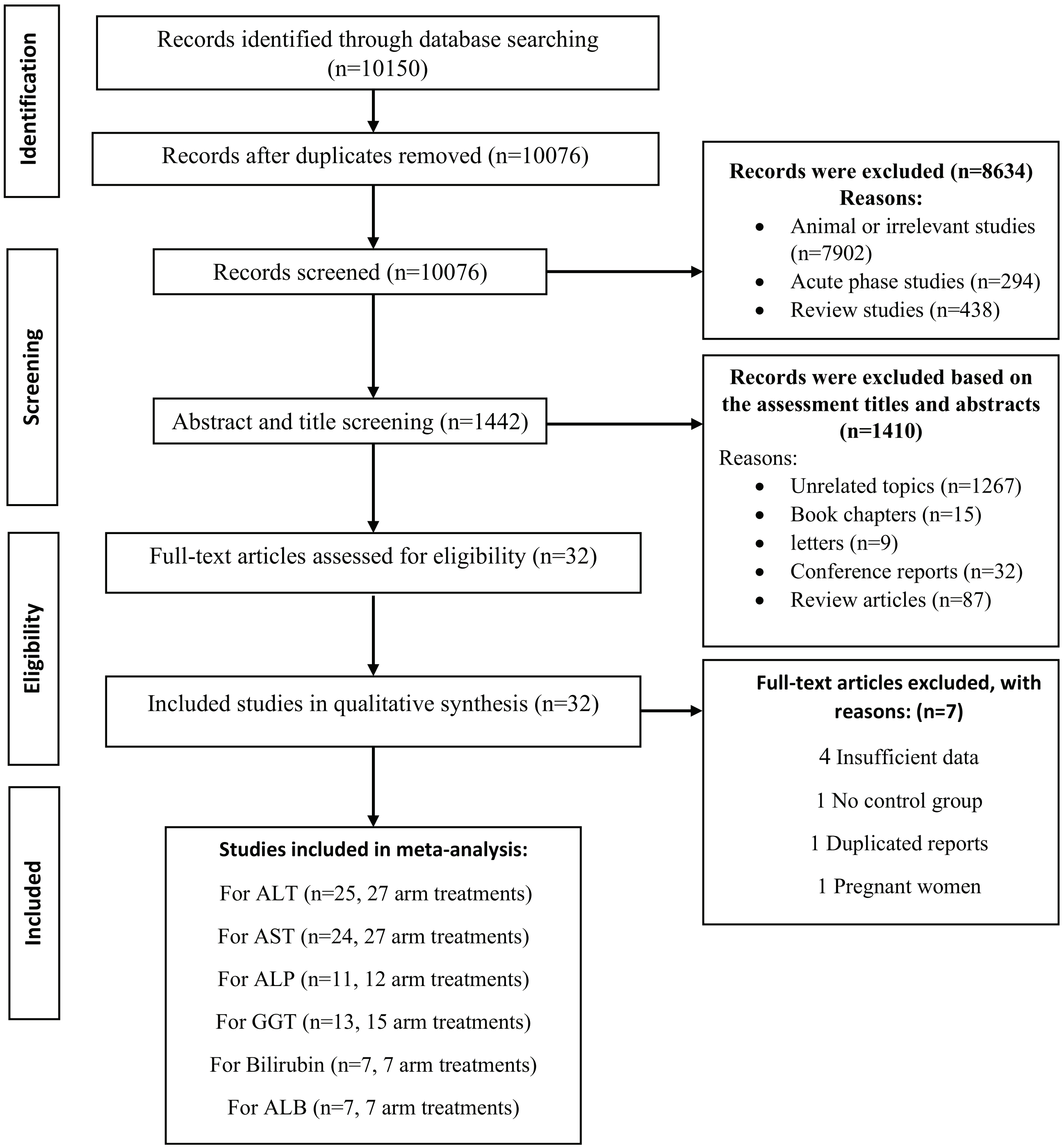

Figure 1. Flow chart of the process of the study selection.

determined that ALP was reduced in participants with BMI≥30 (MD: −2.61 U/L, −9.92 to 4.71, P=0.458), when using a viscous fiber type (MD: −1.07 U/L, −5.51 to 3.37, P=0.636), and in diabetes participants (MD: −10.71 mg/dL, −14.48 to −9.95) ESM 1, Table E4.

The overall pooled effect size was not affected by any individual studies based on sensitivity analysis. No indication of publication bias using the Egger's test (P=0.760) or Begg's test (P=0.837) was found.

Each 5 g/d increment in soluble fiber dose increased ALP level by 0.06 U/L (−0.33 to 0.21, P=0.673; I^2=0.0%, P=0.549) Table 2. Dose-response analysis showed a linear decrease in ALP level to 20 g/d (MD 20g/d: −0.22, 95% CI: −1.63, 1.18). ESM 1, Figure E1 and Table E5. The pooled mean difference of 13 studies (15 treatment arms) including 853 participants (432 cases and 421 controls) indicated that soluble fiber supplementation might not significantly affect GGT levels compared to placebo (MD: 0.12 U/L; 95% CI:

Table 2. The effect of soluble fiber supplements on liver function

	Pairwise meta-analysis					Dose-response meta-analysis					
	Studies, n	WMD (95% CI)	P value	I^2, %	$P_{heterogeneity}$	Dose, g/d	Studies, n	WMD (95% CI)	P value	I^2, %	$P_{heterogeneity}$
ALT	27	−0.02 (−1.06, 1.01)	0.962	13.6	0.263	5	27	0.33 (−0.10, 0.76)	0.130	4.9	0.392
AST	27	−0.34 (−0.84, 0.15)	0.177	0.0	0.661	5	27	−0.06 (−0.33, 0.21)	0.673	0.0	0.549
ALP	12	0.29 (−0.14, 0.71)	0.188	0.0	0.926	5	12	0.06 (−0.03, 0.14)	0.185	0.0	0.926
GGT	15	0.12 (−0.81, 1.05)	0.801	0.0	0.995	5	15	−0.03 (−0.36, 0.30)	0.851	0.0	0.995
BIL	7	0.42 (−0.08, 0.93)	0.102	0.0	0.872	5	7	0.27 (−0.01, 0.55)	0.063	0.0	0.946
ALB	7	0.64 (−0.42, 1.70)	0.235	78.6	<0.001	5	7	0.35 (−0.23, 0.93)	0.240	77.9	<0.001

Abbreviations: MD: mean difference; CI: confidence interval; ALT: alanine transaminase; AST: aspartate transaminase; ALP: alkaline phosphatase; GGT: gamma-glutamyltransferase; BIL: bilirubin; ALB: albumin.

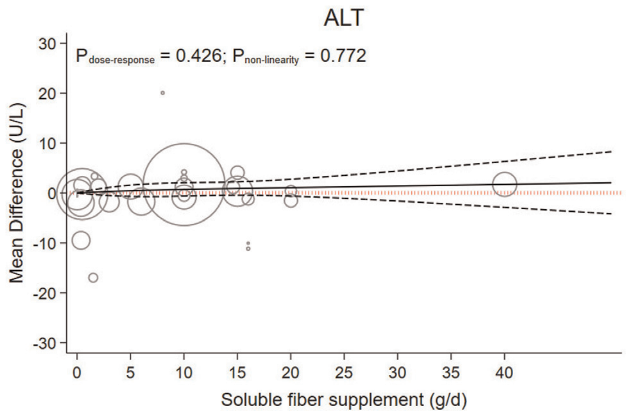

Figure 2. The effects of different doses of soluble fiber supplementation on ALT form the nonlinear dose response meta-analysis.

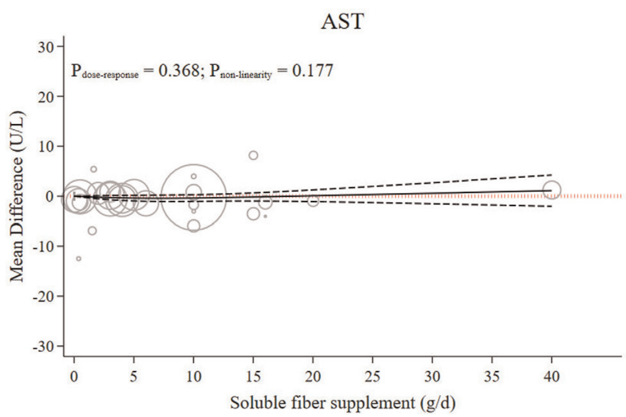

Figure 3. The effects of different doses of soluble fiber supplementation on AST form the nonlinear dose response meta-analysis.

−0.81 to 1.05, P=0.801). Heterogeneity was not detected between the studies (I^2=0.0%, P=0.995) Table 2. Based on subgroup analysis, the effect of soluble fiber supplementation on GGT was greater in studies with longer duration ESM 1, Table E4.

Statistically significant publication bias was not found (p=0.921, Begg's test and P=0.783, Egger's test). The overall pooled effect size was not affected by any individual studies based on sensitivity analysis.

Each 5 g/d increment in soluble fiber supplementation decreased GGT concentrations by −0.03 U/L (−0.36 to 0.30, P=0.851; I^2=0.0%, P=0.995) Table 2. A non-significant association between GGT level and soluble fiber supplementation dosage was observed ($P_{non-linearity}$=0.503, $P_{dose-response}$=0.785) ESM 1, Table E5 and Figure E2.

The effect of soluble fiber supplementation on BIL concentration was examined in seven articles, involved 2491 subjects (258 intervention, 250 placebo). In this regard, soluble fiber supplementation had no significant impact on BIL (MD: 0.42 μmol/L, 95% CI: −0.08 to 0.93, P=0.102). Between-study heterogeneity was low (I^2=0.0%, P=0.872) Table 2.

Based on sensitivity analysis, exclusion of any single studies from the analysis did not alter the overall effect. No evidence of publication bias was found using Begg's (P=1) and Egger's test (P=0.175).

Each 5 g/d increment in soluble fiber supplementation increased BIL by 0.27 μmol/L (−0.01 to .55, P=0.063; I^2=0.0%, P=0.946) Table 2. Dose-dependent effects showed a non-significant reduction in BIL ($P_{non-linearity}$= 0.823, $P_{dose-response}$=0.174) ESM 1, Figure E3.

Using data from 7 studies containing 599 participants (305 case and 294 control), meta-analysis suggested that soluble fiber induced a non-significant increase in ALB levels (MD: 0.64 g/dl, 95% CI: −0.42 to 1.70, P=0.235), with significant between-study heterogeneity (I^2=78.6%, P<0.001) Table 2.

Subgroup analysis suggested that stratification based on dose and study population could explain this heterogeneity. Also, the effect size was more pronounced in studies that had a soluble fiber supplementation ≥10 gram per day (MD: 0.99 g/dl, 95% CI: −0.63 to 2.61, P=0.230) and trials that used viscous fiber as supplementation (MD: 1.55 g/dl, 95% CI: −0.69 to 3.78) ESM 1, Table E4.

The overall pooled effect size was not affected by any individual studies based on sensitivity analysis. Publication bias was not significant in Begg's (P=0.764) and Egger's test (P=0.323).

Each 5 g/d increment in soluble fiber supplementation increased ALB concentrations by 0.35 g/dl (−0.23 to

0.93, P=0.240; I^2=77.9%, P<0.001) Table 2. Dose-response analysis suggested that soluble fiber supplementation had no significant effect on ALB level ($P_{non-linearity}$=0.780, $P_{dose-response}$=0.448) ESM 1, Table E5 and Figure E4.

Details of the quality assessment according to the areas used by the Cochrane Collaborations tool were presented in ESM 1, Table E6. Among the studies included in the systematic review, all of studies had good quality exception one study with fair quality [38]. The GRADE approach was applied to evaluate the certainty of the evidence ESM 1, Table E7. The evidence was rated low for ALT, AST, ALP, GGT, and BIL and very low for ALB. The evidence was downgraded for particular variables when notable inconsistency, publication bias, indirectness, and imprecision of reported data were present.

Discussion

The findings from the present systematic review and meta-analysis suggested that soluble fiber supplementation might not improve serum concentrations of liver function test serum biomarkers including serum ALT, AST, ALP, GGT, BIL and ALB levels. We found no significant between-study heterogeneity in any of the study endpoints, except for ALB levels.

To our knowledge, this is the first systematic review and meta-analysis studying the effects of soluble fiber supplementation on liver function tests. Despite our non-significant results regarding the effects of soluble fiber consumption on liver enzymes, soluble fibers exhibited some hepatoprotective effects in some animal and human studies [53, 56]. In a type 2 diabetes rat model, insulin sensitivity and serum levels of ALT, ALB and total protein were improved following 4-week treatment with soluble and insoluble fibers extracted from barley [57]. Also, Hydroxypropyl methylcellulose, a viscous soluble fiber, supplementation was associated with improved glucose control and reduced fatty liver and insulin resistance in obese diabetic rats [56]. In a large cohort study of 485717 retired U. S. participants, higher intake of dietary fiber and whole grain were associated with lower risk of liver cancer and mortality from chronic liver diseases [58].

The biological mechanisms for the possible beneficial impact of dietary fibers on liver function and liver diseases were not clearly elucidated. Dietary fibers have been reported to beneficially affect some metabolic risk factors related to liver diseases including insulin resistance, metabolic syndrome and fat accumulation in the liver [59, 60]. Since, visceral fat mass might play a role in the development of steatosis, soluble fibers may induce their hepatoprotective impact by reducing visceral fat mass [61]. Altered gut microbiota has been linked to the development of some abnormal liver conditions including NAFLD, hepatic steatosis and cirrhosis [62]. The reduction of SCFA-producing bacteria has been suggested to negatively affect inflammatory responses, metabolic pathways and insulin response [63]. Fermentable fibers are major substrates for gut bacterial fermentative activity, and thus SCFAs production [64]. In the liver, SCFAs increase lipid oxidation and energy expenditure, thus ameliorate hepatic steatosis [62]. Increased intestinal permeability following gut dysbiosis and resulting metabolic endotoxemia and inflammation might be involved in the NAFLD or non-alcoholic steatohepatitis (NASH) pathogenesis and progression [65]. Bacterial-derived SCFAs are necessary for maintaining gut integrity and reducing metabolic endotoxemia. Also, SCFAs might improve hepatic steatosis by appetite regulation and promoting insulin sensitivity [66].

The non-significant results of the present study could be explained partly by the discrepancies between included studies in terms of the type and dose of soluble fiber used, baseline health condition of study population, intervention duration and gut microbial composition of study participants at baseline. In fact, the included studies were significantly different with regard to the type of soluble fiber used. Considering other metabolic outcomes such as blood lipid levels, insulin resistance and glycemic control, various soluble fibers have induced different metabolic effects, based on their intrinsic characteristics including fermentability and viscosity [12, 67]. Although, we did not find any significant between-study heterogeneity for different study endpoints, except for ALB level, studies with longer duration or those used viscous soluble fibers have reported greater reductions in liver enzymes based on subgroup analyses, a finding which is in line with other studies investigated metabolic effects of soluble fibers [12]. Also, we only included studies that intervened with one type of soluble fiber. Supplementation with a combination of two or more types of soluble fibers or a combination of non-soluble and soluble fibers might exert different effects on liver function.

We found no significant between-study heterogeneity in any of the study endpoints, except for ALB levels. Sources of heterogeneity included different biases across studies, differences in the design of studies or in participants, interventions, measurements, exposures or outcomes evaluated. Subgroup analysis suggested that stratification based on dose and study population could explain this heterogeneity. However, the number of studies included for ALB levels was limited compared to other endpoints such as ALT, AST and ALP. So, the results of between-study heterogeneity for ALB levels should be interpreted with caution.

The strengths of our study are as follow; in the present comprehensive meta-analysis the beneficial effects of soluble fiber supplementation on liver function parameters has been investigated for the first time; the included studies involved both healthy and non-healthy participants, including patients with NASH, T2D, hyperlipidemia and obesity, so our findings might be generalizable to general population; we tried to minimize the presence of confounding variables by assessing study quality and biases, comprehensively.

This study also has a number of potential limitations which should be discussed. First, since the fiber content of diet was not reported in most included trials, we only considered supplemental soluble fiber in our analyses. This might affect our estimates due to the different fiber content of diet between intervention groups. Second, liver function parameters were measured in most included studies as the secondary outcomes, which might increase the risk of not adjusting confounding factors completely in many of these studies.

Conclusion

Findings from this systematic review meta-analysis did not support the beneficial effects of soluble fiber supplementation on blood ALT, AST, ALP, GGT, BIL and ALB levels. There is a need for future long-term high-quality interventions to examine the effects of different types, sources and doses of soluble fibers on liver function test serum biomarkers as primary outcomes. Also, the mechanisms of the potential effects of dietary fibers on liver function require further investigation.

Electronic supplementary material

The following electronic supplementary material is available with this article at https://doi.org/10.1024/0300-9831/a000800

ESM 1. Electronic supplementary material containing Supplementary Tables E1 to E7 and Supplementary Figures E1 to E4.

References

1. Li S, Tan HY, Wang N, Cheung F, Hong M, Feng Y. The potential and action mechanism of polyphenols in the treatment of liver diseases. Oxid Med Cell Longev. 2018;2018:8394818.
2. Li S, Hong M, Tan H-Y, Wang N, Feng Y. Insights into the role and interdependence of oxidative stress and inflammation in liver diseases. Oxid Med Cell Longev. 2016;2016:4234061.
3. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol. 2019;70:151–71.
4. Wiegand J, Berg T. The etiology, diagnosis and prevention of liver cirrhosis: part 1 of a series on liver cirrhosis. Dtsch Arztebl Int. 2013;110:85–91.
5. Jara M, Dziodzio T, Malinowski M, Lüttgert K, Nikolov R, Ritschl PV, et al. Prospective Assessment of Liver Function by an Enzymatic Liver Function Test to Estimate Short-Term Survival in Patients with Liver Cirrhosis. Dig Dis Sci. 2019;64:576–84.
6. Li S, Tan HY, Wang N, Zhang ZJ, Lao L, Wong CW, et al. The role of oxidative stress and antioxidants in liver diseases. Int J Mol Sci. 2015;16(11):26087–124.
7. Yao B, Fang H, Xu W, Yan Y, Xu H, Liu Y, et al. Dietary fiber intake and risk of type 2 diabetes: a dose-response analysis of prospective studies. Eur J Epidemiol. 2014;29:79–88.
8. Du P, Luo K, Wang Y, Xiao Q, Xiao J, Li Y, et al. Intake of dietary fiber from grains and the risk of hypertension in late midlife women: results from the SWAN study. Front Nutr. 2021;8:730205.
9. McRae MP. Dietary fiber is beneficial for the prevention of cardiovascular disease: an umbrella review of meta-analyses. J Chiropr Med. 2017;16:289–299.
10. Slavin JL. Position of the American Dietetic Association: health implications of dietary fiber. J Am Diet Assoc. 2008;108:1716–31.
11. Kim Y, Je Y. Dietary fiber intake and total mortality: a meta-analysis of prospective cohort studies. Am J Epidemiol. 2014;180:565–73.
12. Xie Y, Gou L, Peng M, Zheng J, Chen L. Effects of soluble fiber supplementation on glycemic control in adults with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2021;40:1800–10.
13. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr. 1999;69:30–42.
14. Thompson SV, Hannon BA, An R, Holscher HD. Effects of isolated soluble fiber supplementation on body weight, glycemia, and insulinemia in adults with overweight and obesity: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr. 2017;106:1514–28.
15. Amar MJ, Kaler M, Courville AB, Shamburek R, Sampson M, Remaley AT. Randomized double blind clinical trial on the effect of oral α-cyclodextrin on serum lipids. Lipids Health Dis. 2016;15(1):115.
16. Bomhof MR, Parnell JA, Ramay HR, Crotty P, Rioux KP, Probert CS, et al. Histological improvement of non-alcoholic steatohepatitis with a prebiotic: a pilot clinical trial. Eur J Nutr. 2019;58:1735–45.
17. Cicero AFG, Fogacci F, Veronesi M, Strocchi E, Grandi E, Rizzoli E, et al. A randomized placebo-controlled clinical trial to evaluate the medium-term effects of oat fibers on human health: the Beta-Glucan Effects on Lipid Profile, Glycemia and inTestinal Health (BELT) study. Nutrients. 2020;12(3):686.
18. Daubioul CA, Horsmans Y, Lambert P, Danse E, Delzenne NM. Effects of oligofructose on glucose and lipid metabolism in patients with nonalcoholic steatohepatitis: Results of a pilot study. Eur J Clin Nutr. 2005;59:723–6.
19. Evans M, Falcone PH, Crowley DC, Sulley AM, Campbell M, Zakaria N, et al. Effect of a Euglena gracilis fermentate on immune function in healthy, active adults: A randomized, double-blind, placebo-controlled trial. Nutrients. 2019;11(12):2926.
20. Farhangi MA, Javid AZ, Dehghan P. The effect of enriched chicory inulin on liver enzymes, calcium homeostasis and hematological parameters in patients with type 2 diabetes mellitus: A randomized placebo-controlled trial. Prim Care Diabetes. 2016;10:265–71.
21. Gonai M, Shigehisa A, Kigawa I, Kurasaki K, Chonan O, Matsuki T, et al. Galacto-oligosaccharides ameliorate dysbiotic Bifidobacteriaceae decline in Japanese patients with type 2 diabetes. Beneficial Microbes. 2017;8:705–16.
22. Hokazono H, Omori T, Yamamoto T, Akaoka I, Ono K. Effects of a fermented barley extract on subjects with slightly high

serum uric acid or mild hyperuricemia. Biosci Biotechnol Biochem. 2010;74:828–34.
23. Kitagawa M, Nakagawa S, Suzuki T, Kishimoto Y, Kanahori S, Hatakeyama Y, et al. Visceral fat-reducing effect and safety of continuous consumption of beverage containing resistant maltodextrin: A randomized, double-blind, placebo-controlled, parallel-group clinical trial. J Nutr Sci Vitaminol. 2020;66:417–26.
24. Lee YJ, Paik DJ, Kwon DY, Yang HJ, Park Y. Agrobacterium sp.-derived β-1,3-glucan enhances natural killer cell activity in healthy adults: a randomized, double-blind, placebo-controlled, parallel-group study. Nutr Res Pract. 2017;11:43–50.
25. Sakai C, Abe S, Kouzuki M, Shimohiro H, Ota Y, Sakinada H, et al. A randomized placebo-controlled trial of an oral preparation of high molecular weight fucoidan in patients with type 2 diabetes with evaluation of taste sensitivity. Yonago Acta Medica. 2019;62:14–23.
26. Shimada M, Nagano N, Goto S, Ito K, Tsutsui T, Ando T, et al. Effect of polydextrose intake on constipation in Japanese dialysis patients: A triple-blind, randomized, controlled trial. J Nutr Sci Vitaminol. 2015;61:345–53.
27. Tayebi Khosroshahi H, Vaziri ND, Abedi B, Asl BH, Ghojazadeh M, Jing W, et al. Effect of high amylose resistant starch (HAM-RS2) supplementation on biomarkers of inflammation and oxidative stress in hemodialysis patients: a randomized clinical trial. Hemodial Int. 2018;22:492–500.
28. Park H, Lee E, Kim Y, Jung H, Kim K, Kwon O. Metabolic profiling analysis reveals the potential contribution of barley sprouts against oxidative stress and related liver cell damage in habitual alcohol drinkers. Antioxidants. 2021;10(3):459.
29. Hiel S, Gianfrancesco MA, Rodriguez J, Portheault D, Leyrolle Q, Bindels LB, et al. Link between gut microbiota and health outcomes in inulin -treated obese patients: Lessons from the Food4Gut multicenter randomized placebo-controlled trial. Clin Nutr. 2020;39:3618–28.
30. Reimer RA, Wharton S, Green TJ, Manjoo P, Ramay HR, Lyon MR, et al. Effect of a functional fibre supplement on glycemic control when added to a year-long medically supervised weight management program in adults with type 2 diabetes. Eur J Nutr. 2021;60:1237–51.
31. Zhang L, Ouyang Y, Li H, Shen L, Ni Y, Fang Q, et al. Metabolic phenotypes and the gut microbiota in response to dietary resistant starch type 2 in normal-weight subjects: a randomized crossover trial. Sci Rep. 2019;9:4736.
32. Hess AL, Benítez-Páez A, Blædel T, Larsen LH, Iglesias JR, Madera C, et al. The effect of inulin and resistant maltodextrin on weight loss during energy restriction: a randomised, placebo-controlled, double-blinded intervention. Eur J Nutr. 2020;59:2507–24.
33. Roshanravan N, Mahdavi R, Alizadeh E, Jafarabadi MA, Hedayati M, Ghavami A, et al. Effect of butyrate and inulin supplementation on glycemic status, lipid profile and glucagon-like peptide 1 level in patients with type 2 diabetes: a randomized double-blind. Placebo-Controlled Trial. Horm Metab Res. 2017;49:886–91.
34. Buddington RK, Kapadia C, Neumer F, Theis S. Oligofructose provides laxation for irregularity associated with low fiber intake. Nutrients. 2017;9(12):1372.
35. Nourian M, Akbarzadeh Z, Askari G, Marasi M, Rafiee R. The effect of psyllium on anthropometric measurements and liver enzymes in overweight or obese adults with nonalcoholic fatty liver disease (NAFLD). Inflamm Intest Dis. 2017;2(1):1–92.
36. Mosikanon K, Arthan D, Kettawan A, Tungtrongchitr R, Prangthip P. Yeast β-glucan modulates inflammation and waist circumference in overweight and obese subjects. J Diet Suppl. 2017;14:173–85.
37. Chang HC, Huang CN, Yeh DM, Wang SJ, Peng CH, Wang CJ. Oat prevents obesity and abdominal fat distribution, and improves liver function in humans. Plant Foods Hum Nutr. 2013;68:18–23.
38. Gaullier JM, Sleboda J, Øfjord ES, Ulvestad E, Nurminiemi M, Moe C, et al. Supplementation with a soluble beta-glucan exported from Shiitake Medicinal Mushroom, Lentinus edodes (Berk.) Singer Mycelium: A crossover, placebo-controlled study in healthy elderly. Int J Med Mushrooms. 2011;13:319–26.
39. Wolever TMS, Tosh SM, Gibbs AL, Brand-Miller J, Duncan AM, Hart V, et al. Physicochemical properties of oat β-glucan influence its ability to reduce serum LDL cholesterol in humans: A randomized clinical trial. Am J Clin Nutr. 2010;92: 723–32.
40. Cloetens L, Broekaert WF, Delaedt Y, Ollevier F, Courtin CM, Delcour JA, et al. Tolerance of arabinoxylan-oligosaccharides and their prebiotic activity in healthy subjects: A randomised, placebo-controlled cross-over study. Br J Nutr. 2010;103: 703–13.
41. Carabin IG, Lyon MR, Wood S, Pelletier X, Donazzolo Y, Burdock GA. Supplementation of the diet with the functional fiber PolyGlycoplex® is well tolerated by healthy subjects in a clinical trial. Nutr J. 2009;8:9.
42. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. 2009;62:e1–e34.
43. Peng W, Mao P, Liu L, Chen K, Zhong Y, Xia W, et al. Effect of carnosine supplementation on lipid profile, fasting blood glucose, HbA1C and insulin resistance: a systematic review and meta-analysis of long-term randomized controlled trials. 2020;48.
44. Hozo SP, Djulbegovic B, Hozo I, Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5:13.
45. Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. J Clin Epidemiol. 2000;53:1119–29.
46. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011; Available from: www.handbook.cochrane.org
47. Crippa A, Orsini N. Dose-response meta-analysis of differences in means. BMC Med Res Methodol. 2016;16:91.
48. Bretz F, Pinheiro JC, Branson M. Combining multiple comparisons and modeling techniques in dose-response studies. Biometrics. 2005;61:738–48.
49. Nishimura A, Kitazono E, Imose K, Urita Y, Matsui T. Effect of functional barley BARLEYmax (Tantangara) on intestinal regulation: A double-blind, randomized, placebo-controlled parallel group comparison clinical study. Japanese Pharmacol Ther. 2017;45:1047–55.
50. Jakeman S, Henry C, Martin B, McCabe G, McCabe L, Jackson G, et al. Soluble corn fiber increases bone-calcium retention in postmenopausal women in a dose-dependent manner. Am J Clin Nutr. 2016;104(3):837–43.
51. Wolever TMS, van Klinken BJW, Spruill SE, Jenkins AL, Chu Y, Harkness L. Effect of serving size and addition of sugar on the glycemic response elicited by oatmeal: A randomized, crossover study. Clin Nutr ESPEN. 2016;16:48–54.
52. Zabriskie HA, Blumkaitis JC, Moon JM, Currier BS, Stefan R, Ratliff K, et al. Yeast beta-glucan supplementation downregulates markers of systemic inflammation after heated treadmill exercise. Nutrients. 2020;12(4):1144.
53. Kamal E, Kaddam LA, Alagib A, Saeed A. Dietary fibers (gum arabic) supplementation modulates hepatic and renal profile

among rheumatoid arthritis patients, phase II trial. Front Nutr. 2021;8:552049.
54. Benítez-Páez A, Hess AL, Krautbauer S, Liebisch G, Christensen L, Hjorth MF, et al. Sex, food, and the gut microbiota: disparate response to caloric restriction diet with fiber supplementation in women and men. Mol Nutr Food Res. 2021;65:e2000996.
55. Riikonen S, Savonius H, Gylling H, Nikkilä K, Tuomi AM, Miettinen TA. Oral guar gum, a gel-forming dietary fiber relieves pruritus in intrahepatic cholestasis of pregnancy. Acta Obstet Gynecol Scand. 2000;79:260–4.
56. Brockman DA, Chen X, Gallaher DD. Hydroxypropyl methylcellulose, a viscous soluble fiber, reduces insulin resistance and decreases fatty liver in Zucker Diabetic Fatty rats. Nutr Metab (Lond). 2012;9:100.
57. Liu X, Yang W, Petrick JL, Liao LM, Wang W, He N, et al. Higher intake of whole grains and dietary fiber are associated with lower risk of liver cancer and chronic liver disease mortality. Nat Commun. 2021;12:6388.
58. Willmann C, Heni M, Linder K, Wagner R, Stefan N, Machann J, et al. Potential effects of reduced red meat compared with increased fiber intake on glucose metabolism and liver fat content: a randomized and controlled dietary intervention study. Am J Clin Nutr. 2019;109:288–96.
59. Weickert MO, Pfeiffer AFH. Impact of Dietary Fiber Consumption on Insulin Resistance and the Prevention of Type 2 Diabetes. J Nutr. 2018;148:7–12.
60. Daubioul CA, Horsmans Y, Lambert P, Danse E, Delzenne NM. Effects of oligofructose on glucose and lipid metabolism in patients with nonalcoholic steatohepatitis: results of a pilot study. Eur J Clin Nutr. 2005;59:723–6.
61. Zhang S, Zhao J, Xie F, He H, Johnston LJ, Dai X, et al. Dietary fiber-derived short-chain fatty acids: A potential therapeutic target to alleviate obesity-related nonalcoholic fatty liver disease. Obes Rev. 2021;22:e13316.
62. Sanna S, van Zuydam NR, Mahajan A, Kurilshikov A, Vich Vila A, Võsa U, et al. Causal relationships among the gut microbiome, short-chain fatty acids and metabolic diseases. Nat Genet. 2019;51:600–5.
63. Koh A, De Vadder F, Kovatcheva-Datchary P, Bäckhed F. From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. Cell. 2016;165:1332–45.
64. Rau M, Rehman A, Dittrich M, Groen AK, Hermanns HM, Seyfried F, et al. Fecal SCFAs and SCFA-producing bacteria in gut microbiome of human NAFLD as a putative link to systemic T-cell activation and advanced disease. United European Gastroenterol J. 2018;6:1496–507.
65. Liu Y, Wang C, Li J, Li T, Zhang Y, Liang Y, et al. Phellinus linteus polysaccharide extract improves insulin resistance by regulating gut microbiota composition. Faseb J. 2020;34:1065–78.
66. Ho HVT, Jovanovski E, Zurbau A, Blanco Mejia S, Sievenpiper JL, Au-Yeung F, et al. A systematic review and meta-analysis of randomized controlled trials of the effect of konjac glucomannan, a viscous soluble fiber, on LDL cholesterol and the new lipid targets non-HDL cholesterol and apolipoprotein B. Am J Clin Nutr. 2017;105:1239–47.
67. Park H, Lee E, Kim Y, Jung HY, Kim KM, Kwon O. Metabolic profiling analysis reveals the potential contribution of barley sprouts against oxidative stress and related liver cell damage in habitual alcohol drinkers. Antioxidants (Basel). 2021; 10:459.
68. Roshanravan N, Mahdavi R, Jafarabadi MA, Alizadeh E, Ghavami A, Saadat YR, et al. The effects of sodium butyrate and high-performance inulin supplementation on the promotion of gut bacterium Akkermansia muciniphila growth and alterations in miR-375 and KLF5 expression in type 2 diabetic patients: A randomized, double-blind, placebo-controlled trial. Eur J Integr Med. 2018;18:1–7.
69. Akbarzadeh M, Nourian M, Askari G, Maracy MR, Rafiei R. The effect of psyllium on anthropometric measurements and liver enzymes in overweight or obese adults with nonalcoholic fatty liver disease (NAFLD). Int J Adv Biotechnol Res. 2015;33: 1771–83.
70. Gaullier JM, Sleboda J, Øfjord ES, Ulvestad E, Nurminiemi M, Moe C, et al. Supplementation with a soluble β-glucan exported from Shiitake medicinal mushroom, Lentinus edodes (Berk.) singer mycelium: a crossover, placebo-controlled study in healthy elderly. Int J Med Mushrooms. 2011;13:319–26.

History
Received May 4, 2023
Accepted November 8, 2023
Published online December 4, 2023

Conflict of interest
The authors declare that there are no conflicts of interest.

Authors' contribution
A.G., E.N.E., R.Z., S.T., H.M. and H.B. were involved in the conception, design, and conduct of the study and the analysis and interpretation of the results. R.Z., A.G. and H.M. wrote the first draft of the manuscript, and all authors edited, reviewed, and approved the final version of the manuscript. R.Z. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

ORCID
Hanieh Barghchi
https://orcid.org/0000-0002-3503-5540

Rahele Ziaei, Ph.D.
Department of Community Nutrition
School of Nutrition and Food Science
Isfahan University of Medical Sciences
Isfahan, Iran
r.ziaei92@gmail.com

