Effects of Oolong Tea on Postprandial Triglyceride Levels

—Systematic Review and Meta-analysis—

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ABSTRACT

Objective The aim of this systematic review was to synthesize data from randomized controlled trials (RCTs) investigating the effects of oolong tea on postprandial triglyceride (TG) levels.

Methods A literature search was performed using the electronic databases of PubMed, Cochrane Library, EMBASE, Ichushi-Web (Japan), JDreamIII (Japan), and Thai-Journal Citation Index (TCI) search (Thailand). We detected 233 related literature articles in the databases. Of these, two studies fulfilled the eligibility criteria of our study.

Results A total of 50 participants from the two studies fufilled the selection criteria, and the interventions of both studies were oolong tea rich in oolong tea polymerized polyphenols (OTPP). OTPP dosage ranged from approximately 70 mg and resulted in a significantly more pronounced decrease in postprandial TG levels at the 4th hour after a high-fat meal intervention (mean difference (MD): −18.87 mg/dL, (95% confidence interval (CI) −22.92 to −14.82), $P<0.00001$, $I^2=0\%$, $n=2$ trials) and also at the 5th hour after a high-fat intervention (MD: −12.24 mg/dL, (95% CI −16.47 to −8.01), $P<0.00001$, $I^2=0\%$, $n=2$ trials) as compared with controls, respectively.

Conclusion The current systematic review provides some evidence that oolong tea, especially OTTP-enriched oolong tea, may have a beneficial effect on postprandial serum TG levels. However, the data are limited and the included trials had methodological limitations. Results from large, rigorously designed RCTs are needed to assess the effect of oolong tea consumption on postprandial serum TG levels.

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KEY WORDS Oolong tea, Oolong tea polymerized polyphenols, Postprandial, Triglyceride

INTRODUCTION

Over recent decades, there have been large changes in modern lifestyles, and both nutrition habits and physical inactivity have adversely affected public health. Obesity, diabetes, and metabolic syndrome are now relatively common. One outstanding result is the prolonged and exaggerated state of postprandial hyperlipidemia due to the ingestion of multiple fat-rich meals during the day. Fats ingested from meals, etc., are

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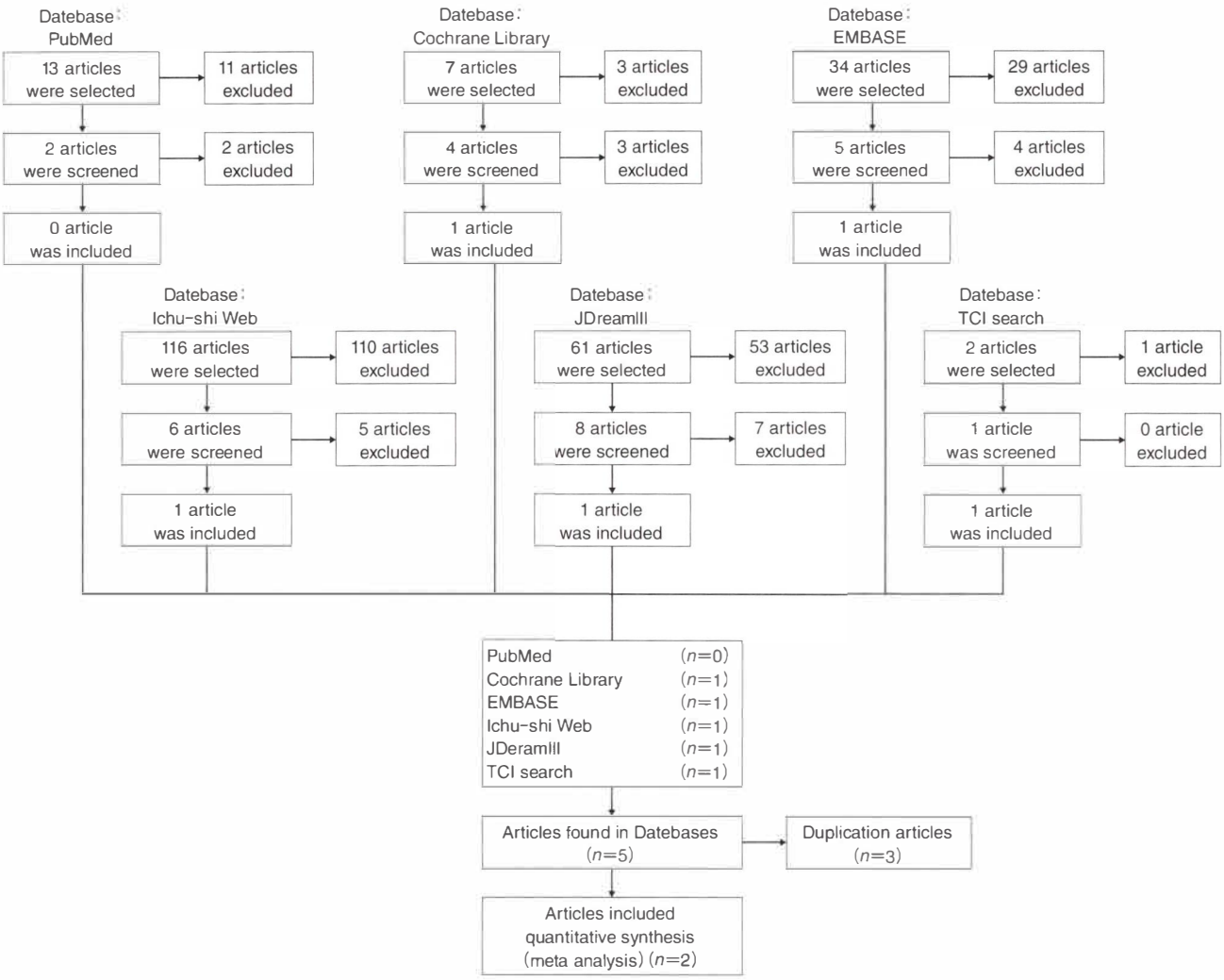


Fig. 1 Flow diagram of the study search and selection process

In the primary screening, the relevancy of the publications was assessed based on the title and abstract. In the secondary screening the studies were evaluated based on the main text.

micellized by the lipase secreted from the pancreas into the gastrointestinal tract and absorbed in the small intestine. This is then transported into the body as lipoprotein and stored as subcutaneous fat and visceral fat. The accumulation of excess fat, subcutaneous and visceral, leads to obesity.[1] Postprandial (non-fasting) hyperlipidemia refers to a condition in which the blood levels of exogenous triglyceride (TG) are elevated. This is a risk factor for cardiovascular disease (CVD), such as atherosclerosis.[2-9] As such, it is important to decrease serum TG levels under not only fasting conditions, but also non-fasting (postprandial) conditions.

Tea is one of the most popular beverages in Asia and is traditionally considered to have a healthy effect. Recently, the ingredients that make up tea have been a focus of interest. Tea is an extract obtained from *Camellia sinensis L.* leaves and is roughly classified into three types: the first is green tea, which is nonfermented; second is black tea, which is fermented; and third is oolong tea, which is semi-fermented.[1] Along with the characteristic scent produced by both the enzymatic and thermal reactions of tea leaves, polymerized polyphenols are produced from catechins through various polymerization processes. These polymerized polyphenols inhibit pancreatic lipase activity, which plays an important role in the fat absorption process.[10] The structure activity relation-

ship of polyphenols contained in oolong tea for lipase inhibition has been investigated. The activity of a dimer (oolonghomobisflavan) was higher than that of a monomer [(-)-Epigallocatechin 3-*O*-gallate (EGCG)]; when the catechin gallate ester was enzymatically degraded, the inhibitory activity decreased. These results suggest that lipase inhibition requires polymerization and the presence of gallate ester groups. Whereby many polymerized polyphenols with gallate ester groups are present in oolong tea, the lipase inhibitory action is thought to be useful.[1] Therefore, we focused on evaluating the relationship between oolong tea and postprandial blood TG. In this study, we systematically reviewed the relationship between oolong tea and postprandial blood TG in healthy humans from the standpoint of preventing negative health effects caused by an excess intake of fat from meals.

METHODS

This study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This review protocol was designed by an experienced information specialist and reviewed by two corresponding authors (the protocol has not been registered).

1 Literature review

Articles were extracted using the electronic databases for PubMed (1946-June 2017), Cochrane Library (thru June 2017), EMBASE (thru June 2017), Ichushi-Web (1977-June 2017), JDreamIII (JSTPlus: 1981-June 2017, JMEDPlus: 1981-June 2017, JST7580: 1975-1981), and TCI search (2014-June 2017). The following keywords were used: "oolong tea" and ("triglyceride" or "triglycerides" or "triglycerol" or "triglycerols" or "triacylgycerol" or "triacylglycerols"). References of the included studies were also scanned for potentially relevant articles. No restrictions were placed on the publication language.

2 Study selection

The following inclusion criteria were defined prior to the study selection process:

(1) Participants: healthy adult males and females including those with mild hypertriglyceridemia (fasting serum TG levels from 150 to 250 mg/dL).
(2) Intervention: oolong tea intake simultaneous with meals
(3) Comparison: placebo intake
(4) Outcome: postprandial serum TG levels
(5) Study design: RCT, quasi-RCT, non-RCT, and crossover.

Two reviewers independently assessed the titles and abstracts of all the reports identified by the electronic and manual searches. Subsequently, the full text of potential articles that met the inclusion criteria were screened, and a final decision was made. Disagreement was resolved by consulting an additional reviewer.

3 Risk of bias assessment

The Cochrane collaboration tool for assessing risk of bias was used to elucidate the risk of bias of the included studies, attaching either low (green), unclear (yellow), or high (red) risk of bias to seven domains (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias) for each study.[11]

4 Data extraction and analyses

Data extracted from each trial were: reference, sample size, male/female(*n*/*n*), age[years, mean±SD], BMI (mean±SD), duration (hours), design, diseases/health status/medication, high-fat intervention, oolong tea intervention, comparison group, outcome parameter and adverse effects. Any relevant missing information on the trial was sought from the original author(s) of the article, if required. Our two reviewers independently extracted the data from each full-text report using a standard data extraction form.

Two reports were extracted and integrated after examining whether they could be integrated without heterogeneity. All data were analyzed using Review Manager ver. 5.3 as provided by the Cochrane collaboration.[12] The random effect model was used in consideration of individual research variability. Using the random effects model, we compared the post-mean values or the changes from baseline values and corresponding SD of the intervention and control/intervention groups. Pooled effects of the different interventions were investigated as MD. Heterogeneity between trial results was tested using a standard χ^2 test. The I^2 parameter was used to quantify any inconsistency: $I^2 = ((Q-df))/Q \times 100\%$, where Q is the χ^2 statistic and *df* is its degree of freedom. An I^2-value $>50\%$ was considered to represent considerable heterogeneity. Dichotomous variables were analyzed, assessed and indicated along with *P* values and 95% confidence

intervals（CIs）. We planned to use a test for asymmetry of the funnel plot previously proposed.[13] however, publication bias was not formally assessed using a funnel plot due to the small number of studies（<10）included in the analyses.[14] If appropriate, a meta-analysis was conducted. The data were analyzed using Review Manager ver. 5.3.

RESULTS

1 Literature search and study characteristics

We initially gathered 233 literature articles from the databases. Of the 233 articles, 26 were selected based on the primary（title and abstract）screening. Subsequently, 26 articles were screened in the secondary（full text）screening. Finally, five studies that fit the eligibility criteria were extracted. Of these, three studies were excluded as duplicates, and two remaining studies with a total of 50 participants fulfilled the selection criteria of our study.[15,16] **Fig 1**. summarizes the steps involved in the selection process.

We examined risk of bias in each paper and did not find any domains whose risk of bias was high（red）. Almost all domains showed a low（green）risk of bias risk, although some domains were rated as having some risk of bias（yellow）because various aspects were unclear. In total, both studies were assessed as having an "overall low risk of bias". The result of the risk of bias for each domain in both studies is summarized in **Fig. 2**.

Considering clinical and methodological heterogeneity, it was reasonable to do a meta-analysis. We conducted meta-analyses for outcome at the 4th and 5th hour after consumption of a high-fat meal. This time period was chosen because serum TG peaks at between 4 to 5 hours after having a meal. Study characteristics are summarized in **Table 1**. There was no missing data in the included studies.

2 Postprandial serum triglyceride

Hara Y, et al. reported that postprandial serum TG elevation was significantly suppressed at the 3rd and 5th hours after ingestion of a high-fat meal by drinking an OTPP-enriched oolong tea beverage compared with the placebo beverage（$P<0.05$）. Also, the area under the curve of the serum TG level was significantly decreased（$P<0.05$）. Bumrungpert A, et al. indicated that postprandial serum TG elevation was significantly inhibited at the 2nd, 3rd, 4th, and 5th hours compared with the placebo beverage（$P<0.001$）. Also, the oolong tea significantly decreased the area under the curve of the serum TG level（$P<0.001$）. The meta-analysis showed that there was no problem in statistical heterogeneity. At the 4th hour after a high-fat meal consumption, oolong tea interventions resulted in a significant decrease in serum TG（MD: −18.87 mg/dL,(95%CI: −22.92 to −14.82), $P<0.00001$, $I^2=0\%$）as compared with the respective controls（**Fig. 3**）. A similar result was obtained from the data at the 5th hour（MD: −12.14 mg/dL,(95% CI: −16.47 to −8.01), $P<0.00001$, $I^2=0\%$）（**Fig. 4**）.

3 Adverse effects

Both RCTs reported on adverse effects. No adverse effect was found in one RCT.[15] The severity of symptoms was reported in the other RCT, however, there were no significant differences in any of the observed symptoms between the intervention group and placebo group.[16]

DISCUSSION

Our meta-analysis clearly demonstrated that oolong tea reinforced with OTPP, approximately 70 mg, suppresses the elevation of TG in blood after a high-fat meal intake in healthy adult males and females, including those with mild hyperlipidemia. In addition, the effect of suppressing TG elevation in postprandial blood by OTPP-enriched oolong tea was seen at 4-5 hours when the postprandial TG showed a maximum value.

All clinical trials considered in the eligibility criteria utilized OTPP-enriched oolong tea. OTPP is a group of polyphenols specific to oolong tea wherein catechin is polymerized in the process of semi-fermentation. Nakai, et al. found that OTPP could interfere with fat absorption via inhibition of lipase activity *in vitro*.[1] In addition, Han, et al. reported that oolong tea prevents obesity in a high-fat diet by inhibiting the lipase activity of the pancreas in mice.[17] Furthermore, Toyoda-Ono, et al. reported inhibitory effects of OTPP on postprandial TG after a high-fat diet load in mice and rats.[18] Nakai, et al. showed that OTPP suppressed both serum TG elevation and lymphatic TG absorption under a high-fat dietary condition in mice and rats.[10] Furthermore, Hsu, et al. showed that polyphenol-enriched oolong tea increases lipid excretion into feces when ingesting a high-fat diet in healthy humans.[19]

As described above, OTPP inhibits pancreatic lipase, suppresses the absorption of lipids in the gastrointestinal tract, and is excreted in feces, which is

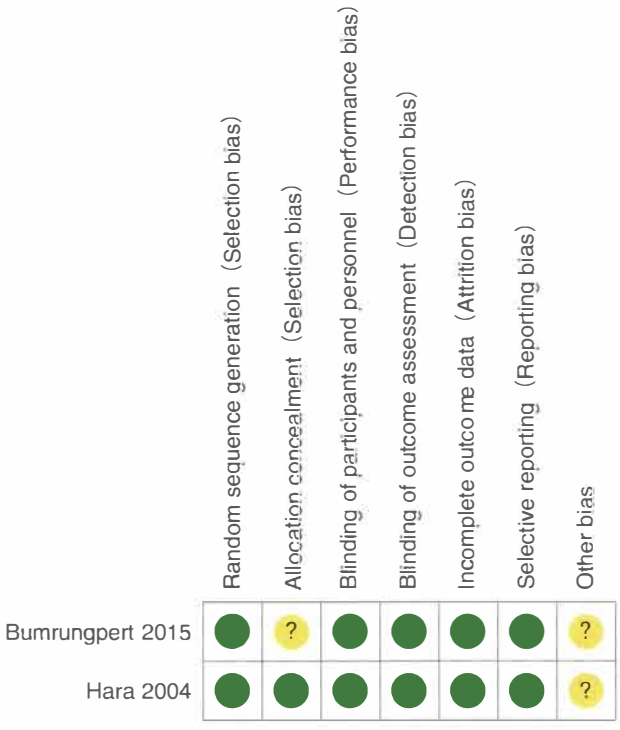


Fig. 2 Risk of bias summary

For each study, every bias domain was evaluated. Review author judgements about each risk of bias item are for each included study. Green means low risk, yellow means unclear risk and red means high risk.

thought to suppress postprandial serum TG elevation. Our systematic review and meta-analysis results suggested that OTPP-enriched oolong tea suppressed a postprandial TG increase in humans, which did not contradict previously reported results.

In recent years, it is becoming clear that the rise in blood TG after a meal (not fasting), rather than fasting TG is a risk factor of CVD, especially for arteriosclerosis. The need to suppress the blood TG value under not only a fasting condition, but also a non-fasting (postprandial) condition has been considered. The results of our systematic review and meta-analysis suggested that OTPP-enriched oolong tea suppressed the elevation of postprandial TG in humans, which may lead to a reduced risk of CVD such as arteriosclerosis.

Excessive fat ingestion from meals, etc., are absorbed and stored as subcutaneous fat and visceral fat. The accumulation of excessive fat results in obesity. Various products have been developed to prevent weight gain, such as Orlistat. Orlistat is an agent that inhibits pancreatic lipase like OTPP and is used as an anti-obesity agent. Orlistat is a medicine that inhibits pancreatic lipase, thereby suppressing the absorption of fat contained in a meal from the gastrointestinal tract and provides a weight reduction effect. However, side effects including fatty stools, increased number of defecations, loose stools, etc., have been reported in Orlistat.[20] Although the mechanism of OTPP is similar to Orlistat, such side effects are not observed in oolong tea that includes OTPP. Therefore, OTPP-enriched oolong tea may be considered as a beneficial and safe alternative that can be taken with every meal to suppress the absorption of fat.

A population-based case-control study to evaluate the association between consumption of tea, especially oolong tea, and risk of dyslipidemia was conducted in Shantou, China, from 2010 to 2011.[21] The study indicated that in the population who had taken oolong tea for a long period, lipid related items such as blood TG were lower and suggested that this may be related to the risk reduction for dyslipidemia. In this meta-analysis, we focused on the effects of single oolong tea ingestion on postprandial blood TG in

Table 1 Characteristics of randomized controlled trials included in the systematic review

Reference	Sample Size, Male/Female (*n*/*n*)	Age (years, Mean±SD)	BMI (kg/m^2, Mean±SD)	Duration (hours), Design	Diseases/ Health Status/ Medication	High-fat Intervention	Oolong Tea Intervention
Hara Y, et al. 2004	22 (12/10)	49.7±8.9	25.9±3.8	5, Crossover	Borderline to mild hypertriglyceridemia (TG 100-250 mg/dL)	Fat enriched corn soup (containing 40 g of fat, 434 kcal)	OTPP enriched oolong tea (OTPP 277.1 μg/mL)
Bumrungpert A, Chongsuwat R. 2015	30 (15/15)	36.5±11.31	25.79±4.40	5, Crossover	Borderline to mild hypertriglyceridemia (TG 100-250 mg/dL)	Corn soup (containing 40 g of fat)	Oolong tea (OTPP 140 μg/mL)

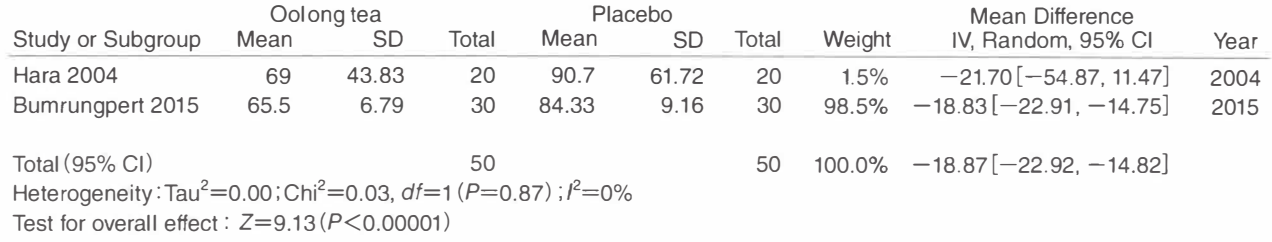


Fig. 3 Effects of oolong tea on post prandial serum TG levels (mg/dL) at the 4th hour after a high-fat meal intake
Forest plot showing pooled MD with 95% CI for two RCTs. For each study, the shaded square represents the point estimate of the intervention effect. The horizontal line joins the lower and upper limits of the 95% CI of these effects. The shaded square area reflects the relative weight of the study in the respective meta-analysis. The diamond at the bottom of the graph represents the pooled MD with the 95% CI for all study groups.

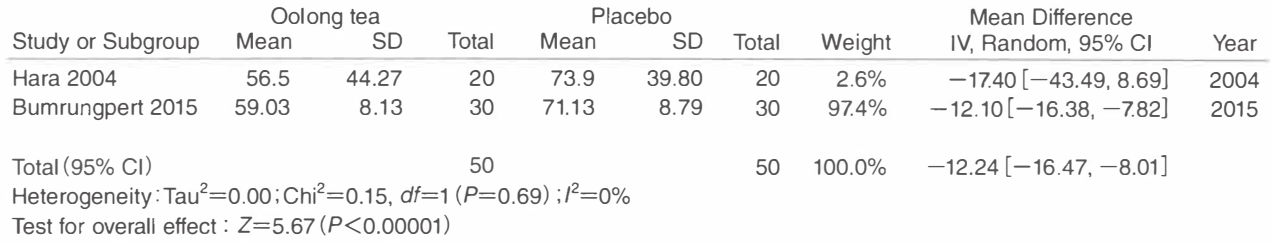
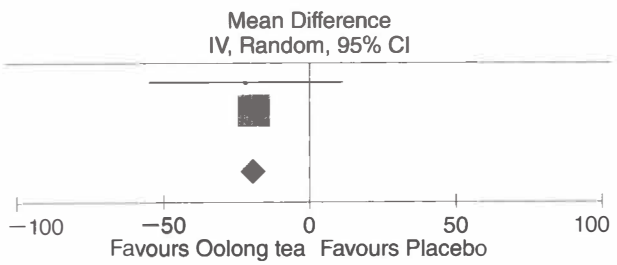


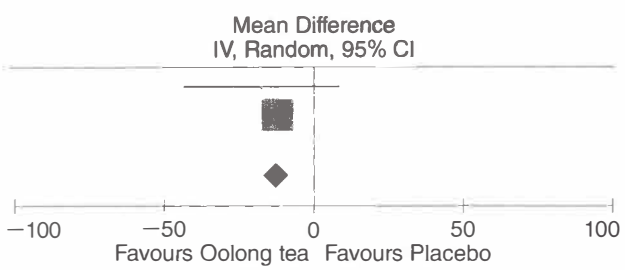
Fig. 4 Effects of oolong tea on post prandial serum TG levels (mg/dL) at the 5th hour after a high-fat meal intake
Forest plot showing pooled MD with 95% CI for two RCTs. For each study, the shaded square represents the point estimate of the intervention effect. The horizontal line joins the lower and upper limits of the 95% CI of these effects. The shaded square area reflects the relative weight of the study in the respective meta-analysis. The diamond at the bottom of the graph represents the pooled MD with the 95% CI for all study groups.

healthy subjects, so long-term effects are unknown. However, the ingestion of OTPP-enriched oolong tea with every meal leads to a suppression in the elevation of postprandial TG, and thus may contribute to the prevention of negative health effects induced by excess fat intake during meals.

Generally, a systematic review has some major limitations. When the sample size of each RCT is small, by integrating multiple RCTs into meta-analysis, the sample size increases and a higher level of evidence can be provided. However, in this review, there were only two studies satisfying the eligibility criteria, and thus the total sample size was still small after integration, and the possibility of publication bias could not be denied. Additionally, although there were no problems with heterogeneity, it is understood that when making a generalization, the number of subjects was small. Therefore, further research with larger sample sizes is necessary.

Comparison Group	Outcome Parameter	Adverse effects
Control beverage (OTPP 33.7 μg/mL)	Serum triglyceride	No Advese effects
Placebo drink (OTPP 0 μg/mL)	Serum triglyceride	No significant difference between oolong tea and placebo





CONCLUSIONS

The current systematic review provides some evidence that oolong tea, especially OTPP-enriched oolong tea, ranging from 68 mg to 70 mg, may have a beneficial and safe effect on postprandial serum TG levels. However, the data are limited and the included trials had methodological limitations. Results from large, rigorously designed RCTs are needed to assess the effect of oolong tea consumption on postprandial serum TG levels.

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【Author contributions】 Y. S., R. S. and S. F. developed the idea for this SR, S. F. prepared the protocol. Literature search was performed by Y. H. and T. K., while data extraction, analyses, and synthesis were performed by all the authors. S. F. prepared the first draft of the manuscript. Disagreements were resolved by consensus, and all authors read and approved the final manuscript.

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