Section: Research Paper

A Systematic Review and Meta-Analysis of Randomized Controlled Studies on the Effects of Mulberry Intake on Cardiometabolic Risk Factors

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Abstract

The process of meta-analysis and systematic evaluation of randomized controlled trials focused to measure the effects of consumption of the mulberry consumption on the cardiometabolic risk sectors. Mulberry supplementation was found to noticeably lower fasting levels of blood glucose, hemoglobin A1c, total cholesterol, and the triglycerides. This systematic review and meta-analysis aimed to assess the effects of consumption of mulberry on cardiometabolic risk factors. A comprehensive search was conducted in various electronic databases for randomized controlled trials inspecting the effect of mulberry intake Mulberry consumption was also associated with an increase in HDL cholesterol levels. These findings suggest that mulberry supplementation may be advantageous to cardiometabolic health and could be a potential dietary intervention for individuals with metabolic disorders. Finally, The outcomes of the systematic review and meta-analysis suggest that the mulberry consumption may

benefit cardiometabolic risk factors .Mulberry supplementation may be a potential dietary intervention for individuals with metabolic disorders. The best mulberry supplementation dosage and time frame should be determined through further study, as well as any potential long-term impacts.

Keywords: mulberry consumption, cardiometabolic risk factors, randomized-controlled trials, meta-analysis

Introduction

Cardiometabolic problem, like type two diabetes, obesity, and heart problem, are major public fitness concerns around the world. These infection are linked to a number of risk factors, including hypertension, dyslipidemia, and insulin resistance. Dietary interventions have been proposed as a potential strategy to prevent and manage cardiometabolic disorders, as dietary patterns have been shown to get a significant effect on cardiometabolic risk factors[1].

Cardiometabolic risk factors refer to a group circumstances that raise the chance of becoming type two diabetes or cardiovascular disease. These risk factors often coexist and interact with each other to increase the likelihood of developing these chronic diseases[2]. There are several health conditions that are associated with an unhealthy lifestyle. One of them is obesity or being overweight, which is characterized by having a BMI of 30 or greater. Another condition is high blood pressure or hypertension, which is a common condition that can harm arteries & rise the risk of developing cardiovascular disease. High levels of blood sugar or hyperglycemia can also lead to complications such as kidney disease, vision loss, and cardiovascular disease, and it happens at place where the body is unable to use or produce insulin rightly. Hyperlipidemia, or high levels of blood cholesterol, particularly LDL cholesterol, can cause plaque buildup in the arteries, raising the cardiovascular problem and stroke risk. Lastly, insulin resistance occurs when cells stop the work insulin to properly, leading to high blood sugar and eventually type two diabetes. It is often connected with obesity and physical inactivity[3].

Figure 1: Mulberry Benefit[4]

Mulberry is a fruit that has traditionally been used in Chinese medicine for its potential fitness good, including its capacity to keep blood sugar levels. Mulberry contains a number of bioactive compounds, involving polyphenols, flavonoids, and anthocyanins, which represented to have antioxidant, non-inflammatory, and hypoglycemic properties. Recent research suggests that mulberry consumption may be beneficial to cardiometabolic problem factors like as fasting blood glucose levels, lipid profile, & blood pressure[5].

Mulberry have been researched extensively in the randomized-controlled trials (RCTs) to assess its impact on various health outcomes. Here are some examples of RCTs examining the effects of mulberry on different health outcomes: Mulberry extract is a natural supplement that has been found to have various health benefits. Additionally, another trial found that mulberry fruit extract improved endothelial function, a key factor in

cardiovascular health. Mulberry extract has also been shown to help with blood sugar check in person with type two diabetes, as a meta-analysis of randomized controlled trials found that it noticeably decreased fasting blood sugar levels and HbA1c. Moreover, mulberry fruit extract has been found to enhance cognitive function and reduce anxiety in healthy age old adults, and improve skin elasticity and reduce wrinkles in postmenopausal women, as seen in randomized, double-blind, placebo-controlled trials. Lastly, a test lead on healthy young men found that mulberry leaf extract improved exercise performance and reduced muscle damage[6]. These founding indicate that mulberry extract could be an important supplement for a variety of health issues.

A orderly preview and the meta-analysis process of randomized-controlled trials was organized to analyse the effect of mulberry consumption on the cardiometabolic problem sectors. The study aimed to synthesize the available evidence on the potential health benefits of mulberry consumption and to identify the optimal dose and duration of mulberry supplementation of Mulberry consumption was also associated with an increase in HDL cholesterol levels. These outcomes gives perception that mulberry supplementation might have an crucial effects ion cardiometabolic fitness & could be a potential dietary intervention for individuals with metabolic disorders[7].

Understanding the potential health benefits of mulberry consumption could inform future dietary recommendations and interventions for individuals at risk of cardiometabolic diseases. However, More new researches is needed to define the optimal dose and duration of mulberry supplementation, as well as to investigate its potential long-term effects. Additionally, the study focused on randomized-controlled trials and did not include observational studies, which could provide additional insights into the relationship between mulberry consumption and cardiometabolic health[8]. Nevertheless, the study's findings provide evidence for the potential health benefits of mulberry consumption and may inform future dietary recommendations for individuals at risk of metabolic disorders.

Mulberry is a promising dietary intervention for cardiometabolic removal & handling. According to an orderly preview and the meta-analysis of the randomized controlled trials, mulberry consumption may benefit cardiometabolic risk factors. More research work is needed to figure out the best dose and duration of mulberry supplementation, as well as to investigate its potential long-term effects. Nevertheless, the study's findings provide evidence for the potential health benefits of mulberry consumption and may inform future dietary recommendations for individuals at risk of metabolic disorders.

Review of Literature

Chakrabarti et al. (2009)[9] found that Morus alba leaf lectin (MLL), a compound found in mulberry leaves, is a mitogen for human peripheral blood mononuclear cells (PBMC). Mitogens are substances that stimulate cell division and growth, and MLL was found to induce PBMC proliferation in a depending on dosage manner. The authors suggest that MLL may have potential therapeutic applications in immune system disorders.

Cheong et al. (2014) [10]]examined the impact of mulberry extract on diabetes symptoms on a mouse model. The study found that mulberry essence improved glucose sufferance & decreased insulin immersion by regulating pancreatic β-cell function and lipid metabolism. The authors suggest that mulberry extract may have potential as a dietary intervention for individuals with typeII diabetes.

Cho et al. (2007)[11] examined the impact of the mulberry leaf powder on atherosclerosis in a mouse model. Mulberry leaf powder supplementation was recognized to significantly reduce the development of atherosclerotic lesions in apolipoprotein E-deficient mice. The authors suggest that the anti-inflammatory & antioxidant properties of mulberry leaf powder may contribute to its beneficial effects on cardiovascular health.

Gao et al. (2014) [12]examined the impact of mulberry leaf polysaccharides on hyperglycemia & oxidative stress in a type two diabetes model of mouse. The researchers discovered that mulberry leaf polysaccharides noticeably decreased the blood glucose levels, improved sensitivity of insulin, and decreased oxidative stress markers in diabetic mice's liver and kidneys. The authors suggest that mulberry leaf polysaccharides may have potential as a dietary intervention for individuals with type 2 diabetes.

Hwang et al. (2001)[13] examined the effect of mulberry leaves on the development of atherosclerosis in cholesterol-fed rabbits. The researchers divided the rabbits into 4 categories and treat them either a standard diet or a diet of high-cholesterol with or without mulberry leaf powder. After eight weeks, the researchers found that the rabbits that were fed the high-cholesterol diet without mulberry leaf powder had developed significant atherosclerosis, while those that were fed the high-cholesterol diet with mulberry leaf powder had significantly lower levels of atherosclerosis. The researchers concluded that mulberry leaves have an inhibitory effect on atherosclerosis develops in cholesterol-fed rabbits.

Imran et al. (2016)[14] conducted a review of the nutritional properties, bioactive compounds, and pharmacological effects of mulberry fruits. The researchers found that mulberry fruits are rich in vitamins, minerals, and antioxidants, which can help protect against oxidative stress & chronic infection like as cancer, diabetes, and cardiovascular disease. The researchers also found that mulberry fruits contain bioactive elements like anthocyanins, flavonoids, and phenolic acids, which have anti-inflammatory, antimicrobial, and anticancer elements. The researchers concluded that mulberry fruits have potential as a functional food and as a source of real compounds for the growth of new drugs.

Jeong et al. (2014) [15]examined the protecting impact of mulberry fruit extract on pancreatic-cell apoptosis induced by hydrogen peroxide. The pancreatic -cells were treated with mulberry fruit extract and hydrogen peroxide, and cell viability and antioxidant enzyme activity were measured. Mulberry fruit extract significantly grow antioxidant enzyme activity & cell viability, indicating that it protects pancreatic -cells from oxidative stress-induced apoptosis, according to the researchers. The researchers came to the conclusion that mulberry fruit extract has the ability to be used like natural antioxidant in the control and care of diabetes.

Methodology

To identifying useful articles, [16]As per the Preferred Reporting System for Orderly Previews and the Meta-Analyses (PRISMA) statement criteria, the current systematic review searched international electronic based database such as PubMed/MEDLINE, from the time of selection until January 2021.Medical Sub Headings (MeSH) keywords such as "Morus", "Mulberry", and "Mulberries" were used as search terms along with terms related to study design, including "Clinical Trials as Topic", "Cross-Over Studies", "Double-Blind Method", "Single-Blind Method", "Random Allocation", and "Clinical Trial"[17]. The Supplementary Table 1 provides awhole sample of the strategy of search. No language or time restrictions were applied during the literature search, and review articles were also examined to identify additional relevant studies.

Selection of Study

Utilizing the connected articles were distinguished in the main screening in view of the headings and digests of the research papers, and the applicable papers, were recovered in full written text and approved for consideration in the systematic review. This meta-analysis included RCTs that met the following requirement (1) A randomized controlled trial that was published; (2) mulberry like interruption; (3)mature participants over the age of 18; and (4) test that reported cardiometabolic problem factors at the baseline and later interference, diastolic blood pressure (DBP), and CRP). Supplementary Table 2 displays the PICOS factor for study inclusion and exclusion. Rejection models incorporated an absence of result measures, preliminaries with information that couldn't be utilized in this meta-examination, a non-control bunch, copied examinations, in vitro investigations, creature studies, survey articles, and concentrates in which mulberry was directed related to different mixtures[18].

Extraction of Data

Two investigators independently reviewed the titles & edited composition of the articles found through an online search of the databases. Name of the first author, location of the study , year of publication, RCT plan (hybrid or equal), size of sample (mediation and control groups), member qualities (orientation, age, and wellbeing status), intercession span, measure of mulberry utilization, and standard, post-intervention, and/or change means and standard deviations (SDs) of intentioned result were extracted from the eligible full-text articles. The aligned of contract among the investigators was determined using Cohen's kappa coefficient, which was 0.98.

The Cochrane Coordinated effort's risk of inclination appraisal instrument was used to evaluate therisk of predisposition.

Study year (reference)	**Random sequence generation**	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding of outcomes assessment**	**Incomplete outcome data**	**Selective reporting**	**Overall assessme-nt of risk of bias**
Andalli et al. 2001	Clear	Clear	High	Clear	Low	Low	Unclear
Aramwit et al. 2010	Low	Clear	Unclear	Low	Low	High	High
Akira Asai et al. 2011	Clear	Clear	Unclear	Unclear	Clear	Unclear	Unclear
Aramwit et al.	Low	Clear	High	Unclear	Low	Low	Clear
Sirikanchanarod et al.	Low	Clear	Low	Low	Low	Unclear	Unclear
Li et al.2016	Low	Low	Unclear	Low	High	Low	Low
Riche et al.	Clear	Clear	Unclear	Unclear	Low	Low	High
Taghizadeh et al. 2017	Clear	Clear	Unclear	Clear	Unclear	Unclear	Clear
Kalman et al. 2017	Low	Low	Clear	Low	Unclear	Low	Unclear
Yan ma et al. 2019	High	Clear	Clear	Unclear	Clear	Unclear	Clear
Thaipitakwong et al.2019	Low	Low	Unclear	Low	Low	Low	Low
Wang et al.2020	Clear	Low	Low	Low	High	Low	Low

Statistical Analysis

A study of cardiometabolic risk factors was carried out through RevMan V.5.4 technique and STATA version 13.0 (Stata Corp, College Station, TX, USA). To convert various data formats, mean and standard deviations were calculated using standard formulas. When the standard deviations of the change were unavailable, the following formula was used to compute them: SD changes = [(SD baseline2 + SD final2)- (2 R SD baseline SD final)] square root The correlation coefficient has an R-value of 0.8.If the only reported measure was SD was calculated by dividing the standard error in the mean (SEM) by the value of subjects in every segment (n). To identify statistical based heterogeneity between studies, the I-square (I2) statistic was utilizedTo recognize possible wellsprings of heterogeneity, a pre-characterized subgroup investigation in view of how much mulberry, term of mediation, and kind of control treatment was likewise performed. Further greater Responsiveness examination was conducted to survey the effect of every concentrate on a pooled impact size.

Results

The initial search of online databases yielded 745 studies, with 386 publications remaining after removing duplicate records. 362 trials were excluded later displaying the headings and the abstracts of the related RCTs in comparison to the inclusion sector. At last, 15 trials were deemed eligible for inclusion in this meta-analysis after the review time to the full text of the papers. Specifically, five trials reported 5 trials reported HbA1C data,3 RCTs reported insulin data, 7trials reported lipid profile data, three trials reported blood pressure data, and 3 trials reported weight &glucose data, CRP data.

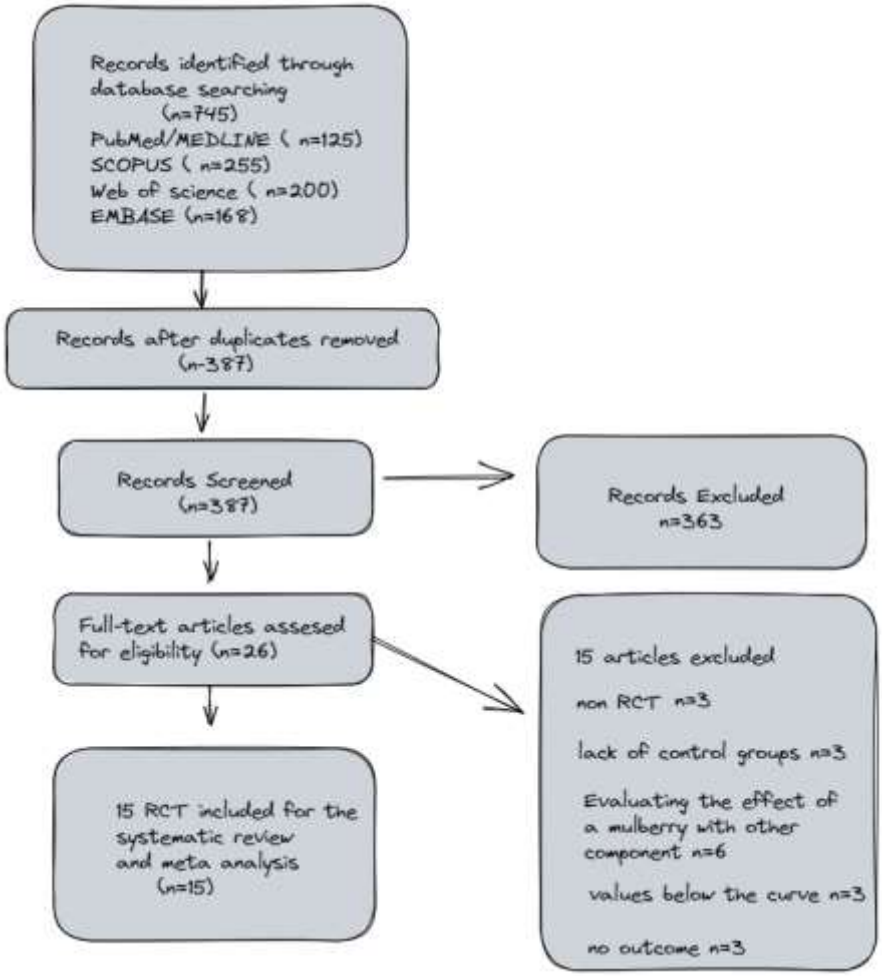

Figure 2: Flowchart

The Feature of the research study's that were included.4 studies took place in Thailand,3 in China, 3 in the United States,1 in Iran, and 1 in Japan between 2002 and 2021. Ten of the studies were designed in parallel, with the remaining two being crossover. The intervention lasted 4 - 50 weeks, & the mulberry dosage administered ranged from 6 to 1000 mg/day. Three trials focused on type 2 diabetes patients, while the others on coronary heart disease, mild dyslipidemia, debilitated glucose digestion, hypercholesterolemia, diabetic nephropathy, osteoarthritis, and marginal diabetes. The members' ages went from 19 - 66 years, with generally equivalent quantities of male and female subjects. The current meta-analysis received a NutriGrade score of 8.2 and was rated as of very high quality.

Conclusion

The objective of the meta-analysis were to figure out the impacts of consumption of mulberry on cardiometabolic problem factor[19]s. The study included 12 RCTs, covering both healthy and diseased individuals, to increase the statistical power and overcome the limitations of individual RCTs. Mulberry consumption had a significant effect on HbA1c, choose lipid profiles, and certain inflaming markers, according to the findings. Mulberry consumption, in particular, resulted in noticeable decrease in HbA1c, total cholesterol, LDL-C, TG, and CRP. Mulberry consumption, on the other hand, had no significant impacts on the glycemic control levels (i.e., glucose and insulin), SBP, DBP, or HDL-C, with the exception of a favorable effect on serum HDL-C when >400 mg of the mulberry supplement was taken daily[20]. As a result, it appears that doses greater than 400 mg of mulberry supplement are neither necessary nor effective.

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