

Review



# The Relationship of Fruits and Fruit-Products Consumption with Glucose Homeostasis and Diabetes: A Comprehensive Update on the Current Clinical Literature

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Abstract: Type 2 diabetes mellitus is a major contributor to morbidity and mortality worldwide. This disease often leads to poor health outcomes, such as neuropathy and diabetic foot ulcers, and increased risk for comorbidities such as cardiovascular complications and renal disease. Lifestyle modifications including diet and physical activity interventions are often explored as prevention and management strategies for T2DM. It is well established that fruits are a rich source of fiber and a variety of phytochemicals, vitamins, minerals, and bioactive compounds that can help optimize human health. Unfortunately, many experts associate the consumption of fruit with a moderate to high glycemic index (GI), which leads to a spike in blood glucose and eventually elevated hemoglobin A1c (HbA1c). The purpose of this comprehensive review is to outline the current clinical literature on the relationship between fruit consumption and various indices of glucose metabolism. A variety of fruits have been clinically studied to determine this relationship, namely in the fresh form (e.g., berries, apples, watermelon, cherries, mangoes), dried fruits (raisins and dates), and juices (derived from cranberry, orange, grape, cherry, and pomegranate). Overall, intake of fruits and fruit-derived products is beneficial for healthy subjects and subjects with T2DM regarding their impact on glucose metabolism and other cardiometabolic markers (e.g., inflammatory responses, lipid profiles). Nonetheless, it is more advisable for diabetic patients to consume fresh or dried fruits rather than fruit-derived products. A special consideration needs to be attributed to both the amount of fruit intake with regards to their respective GI and glycemic load (GL), and when these fruits are consumed. Trials with more a comprehensive design and specific outcomes are required to reveal the mechanisms underlying the beneficial effects of fruit consumption on the T2DM population particularly.

Keywords: fruits; fruit-products; glucose homeostasis; diabetes; T2DM; clinical studies

## 1. Introduction

According to the Centers for Disease Control and Prevention (CDC), more than 90% of Americans diagnosed with diabetes have type 2 diabetes mellitus (T2DM), and it is directly responsible for approximately 1.5 million deaths each year. This has boosted T2DM up to the ninth leading cause of death globally [1,2]. In a recent study by Vinayagam et al., it was revealed that almost 1 in 11 adults between the ages of 20 and 79 years have T2DM worldwide [3]. It is also worth noting that 3.2 million people die annually from complications or diseases associated with diabetes, one common complication being cardiovascular disease [4]. Not to be mistaken for T2DM, type 1 diabetes mellitus (T1DM) is an autoimmune disorder that renders the pancreas unable to produce sufficient levels of insulin, leaving patients reliant on exogenous insulin. T2DM is a chronic disease characterized by increased



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**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). insulin resistance, which impairs glucose homeostasis [5,6], resulting in uncontrollably high blood glucose levels (hyperglycemia). Blood glucose levels remain elevated due to the tissue's inability to properly respond to insulin and absorb glucose from the blood supply, leading to an increase in compensatory insulin production (hyperinsulinemia).

T2DM is primarily treated and managed with pharmacological drugs, such as biguanides and DPP4 inhibitors, which often present a variety of side effects [4,7]. Therefore, lifestyle interventions such as diet and physical activity are often explored as prevention and management strategies for T2DM [8]. Additionally, many experts agree that diet can be a prominent tool in managing and/or preventing T2DM, with a particular interest in optimizing fiber intake. It is well-established that fresh fruits are rich in fiber and a variety of phytochemicals, vitamins, minerals, and bioactive compounds that can help optimize human health [9]. Several international health organizations, including the World Health Organization (WHO), consider fruit an essential food group in a healthy and balanced diet. The WHO recommends an intake of 400 g (five servings of 80 g each) of fruits and vegetables per day, with at least two servings coming from fruit [10]. Similarly, the 2020–2025 Dietary Guidelines for Americans recommend the incorporation of more fruits and vegetables into the daily diets of Americans, suggesting 1.5–2 cup equivalents of fruit and 2–3 cup equivalent of vegetables daily.

Some studies have suggested that the consumption of specific fruits or vegetables, rather than overall fruit and vegetables intake, may have greater health benefits in managing and reducing the risk of T2DM [11]. However, many individuals diagnosed with T2DM have failed to incorporate recommended levels of fruit consumption into their diets. This phenomenon seems to stem from health professionals advising T2DM patients to only consume a maximum of two servings of fruit per day [12], thus spreading fear of fruit and their sugar content. Hence, this review aims to alleviate the fear of negative health consequences and fruit consumption by discussing the current evidence-based clinical literature. The clinical trials we will discuss look at the impacts of acute and chronic consumption of fruits (fresh, dried, juice) on blood glucose levels and other metabolic markers of diabetes. Below is a summary of our recommendations based on published data, which are categorically divided into whole fresh fruit, dried fruit, and fruit juices.

## 2. Methods

This review includes clinical trials with adult subjects, both healthy and T2DM patients, and the outcomes of fruit consumption on their glucose homeostasis and other biomarkers. The literature research was performed on various databases including PubMed, Medline, ScienceDirect, and Google Scholar (latest time accessed 1 April 2023). The search keywords used included: fruit and individual fruit names (e.g., apples, berries, cherries, grapes, mangoes, oranges, watermelon), fruit juice and individual fruit juice names, dried fruit and individual dried fruit names, diet, diabetes, T2DM, glucose, glucose metabolism, glucose homeostasis, body mass index, obesity, total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C). The search was narrowed to English language and human studies including meta-analysis of clinical trials and cross-sectional studies.

#### 3. Fruit and Diabetes

3.1. Whole Fruit

#### 3.1.1. Blueberries

A single 100 g serving of blueberries contains 1.9 g of fiber, of which 1.62 g consist of insoluble fiber [13,14]. These berries are widely known for their richness in multiple phytochemicals, particularly anthocyanins, that have protective effects on health outcomes through their antioxidant capacity [15]. There are numerous studies that have investigated the impacts of blueberry consumption (Table 1), focusing mainly on glucose metabolism [16]. In a double-blind, crossover design study from Bell et al. [17], healthy participants were given a blueberry beverage (prepared out of blueberry powder containing,

respectively, 0 mg, 310 mg, and 724 mg anthocyanins in both sugar-matched and no-addedsugar conditions). Results from this study indicated that acute consumption of blueberry beverages by healthy participants significantly extended the postprandial glucose response, characteristic of an improved glycemic response. In a 6-week intervention study by Stull et al., obese and insulin-resistant subjects consumed a blueberry-based smoothie, which resulted in a significant increase in insulin sensitivity (p = 0.04) [18]. However, when the study was replicated in obese, prehypertensive, and prediabetic subjects, their insulin sensitivity remained unchanged after consuming yogurt- or skim-milk-based blueberry smoothies for 6 weeks [19]. Another 6-month intervention study by Curtis et al. found that consumption of blueberries, irrespective of their form, by adults with metabolic syndrome showed no change in their insulin resistance [20]. A review by Hameed et al. suggests that blueberries should preferably be consumed in whole form because investigating one component at a time is not feasible and meaningful. It is also important to note that whole fruit consumption may offer higher health benefits as many of the fruits' components could work together to exert synergistic effects.

Table 1. A summary of clinical studies examining the glycemic index and intake of whole fruits.

| Fruit                         | Study<br>Design                   | Study Subjects   | Country | Duration  | Fruit<br>Intervention   | Intervention Diet   | Significant<br>Findings   | Reference |
|-------------------------------|-----------------------------------|--|---------|---|---|---|---|-----------|
| Acai berry                    | Pilot study                       | overweight<br>subjects $n = 10$<br>(5 M 5 F) age:<br>28.1 y BMI<br>27.4 $\pm$ 1.8 kg/m <sup>2</sup>  | USA     | 1 month   | 100 g frozen<br>acai pulp   | The participants were<br>instructed to prepare<br>smoothies out of 1 packet<br>of acai pulp, water and<br>up to 4 g of sugar. The<br>smoothies were<br>consumed twice per day.  | Compared to<br>baseline, in<br>fasting glucose<br>and insulin<br>levels following<br>the 30-day<br>treatment.   | [21]      |
| Apple                         | Randomized,<br>crossover          | healthy<br>participants<br>n = 10 (4  M 6 F)<br>age: $24.4 \pm 4.8 \text{ y}$<br>participants with<br>impaired glucose<br>tolerance $n = 9$<br>(6 M 3 F) age:<br>$45.2 \pm 11.1 \text{ y}$ | Japan   | 2 acute<br>consumptions   | Two trials on<br>the same<br>subjects 1:<br>apple<br>consumption<br>after the intake<br>of white rice 2:<br>apple<br>consumption<br>before the<br>intake of white<br>rice | Fasting from 21:00 the<br>night prior test.<br>For each test, packaged<br>white rice (148 g) from<br>the same lot, prepared<br>with 50 g of sugar, and<br>150 g of apple grated<br>with the skin and<br>prepared as 80 kcal for<br>one unit, were used.   | Apple<br>consumption<br>before meals<br>could improve<br>postprandial<br>hyperglycemia<br>in both normal<br>subjects and<br>those with<br>impaired glucose<br>tolerance.  | [22]      |
| Apple,<br>pear, and<br>orange | Acute<br>randomized,<br>crossover | Healthy subjects<br>n = 14 F age:<br>$22.0 \pm 1.3$ y BMI<br>$19.2 \pm 1.2$ kg/m <sup>2</sup>  | China   | 8 meal<br>challenges<br>Each<br>participant<br>tested the 8<br>different meals<br>on 8 different<br>occasions<br>separated by<br>at least one<br>week apart | 15 g of Apple<br>(A), 15 g of Pear<br>(P), 15 g of<br>Orange (O),<br>and cooked rice<br>(R)   | Subjects were instructed<br>to not consume any fruits<br>or fruit products and<br>refrain from coffee, tea,<br>or alcohol, as well as<br>excessive consumption,<br>intensive exercise, and<br>later bedtime on the day<br>prior to each study<br>session.<br>Reference (AC)<br>(W + 50 R): drinking<br>water 30 min before<br>white rice consumption<br>(containing 50.0 g<br>available carbohydrates).<br>Iso-carbohydrate (1) rice<br>preload (15 R + 35 R); (2)<br>orange preload (15 O +<br>35 R); (3) apple preload<br>(15 A + 35 R); (4) pear<br>preload (15 O +<br>35 R); (2) apple preload<br>(15 A + 50 R); (3) pear<br>preload (15 P +<br>50 R).<br>There was a 30 min<br>interval between the<br>preload food and rice<br>meal in both<br>iso-carbohydrate and<br>high-carbohydrate<br>groups. | All the preload<br>treatments,<br>irrespective of<br>iso-carbohydrate<br>or high-<br>carbohydrate<br>meals, resulted<br>in remarkable<br>in incremental<br>peak glucose,<br>of maximum<br>amplitude of<br>glycemic<br>excursion in<br>180 min, also<br>in the area of<br>postprandial<br>glycemic<br>response.<br>Apple elicited<br>the lowest PPGR<br>among all test<br>meals. | [23]      |

| Fruit     | Study<br>Design   | Study Subjects  | Country | Duration   | Fruit<br>Intervention  | Intervention Diet   | Significant<br>Findings   | Reference |
|-----------|---|---|---------|--|--|---|---|-----------|
| Blueberry | Double-blind,<br>randomized<br>placebo-<br>controlled<br>trial          | obese,<br>nondiabetic, and<br>insulin-resistant<br>subjects<br>Blueberry group<br>n = 15 (2  M  13  F)<br>age: $54 \pm 3 \text{ y}$<br>BMI 36.8 kg/m <sup>2</sup><br>Placebo group<br>n = 17 (3  M  14  F)<br>age: $49 \pm 3 \text{ y}$<br>BMI 38 kg/m <sup>2</sup><br>obese with | USA     | 6 weeks  | 45 g<br>freeze-dried<br>blueberries  | Consuming twice/day<br>smoothies Blueberry<br>group: 45 g of<br>blueberries smoothie<br>Control group: identical<br>smoothie without the<br>blueberry powder  | Insulin<br>sensitivity ≯ in<br>the blueberry<br>group at the end<br>of the study  | [18]      |
| Blueberry | Double-blind,<br>randomized,<br>placebo-<br>controlled,<br>parallel arm | prehypertension<br>and prediabetes<br>subjects<br>Blueberry group<br>n = 23 (11 M 12 F)<br>age: 55 $\pm 2$ y BMI<br>35.2 $\pm$ 0.8 kg/m <sup>2</sup><br>Placebo group<br>n = 21 (5 M 16 F)<br>age: 59 $\pm 2$ y<br>BMI 36.0 $\pm$ 1.1<br>kg/m <sup>2</sup>                        | USA     | 6 weeks  | 45 g<br>freeze-dried<br>blueberries  | Consuming 12 oz either<br>yogurt- or skim<br>milk-based smoothies<br>twice/day<br>Blueberry group: 45 g of<br>blueberries<br>Control group: identical<br>smoothie without the<br>blueberry powder   | Insulin<br>sensitivity<br>unchanged   | [19]      |
| Blueberry | Double-blind,<br>crossover,<br>5 conditions,<br>counterbal-<br>anced    | Healthy<br>participants<br>n = 17<br>(4 M 13 F) age:<br>24.1 $\pm$ 4.9 y BMI<br>23.7 $\pm$ 3.6 kg/m <sup>2</sup>  | UK      | Acute<br>consumption<br>in 5 separate<br>mornings                  | Freeze-dried<br>blueberry<br>powder (0, 34,<br>80 g)   | Participants arrived<br>fasting for 2 h and then<br>consumed one of five test<br>condition drinks<br>1: no added sugar 0<br>blueberry,<br>2: sugar matched 0<br>blueberry,<br>3: no added sugar 34 g<br>blueberry,<br>4: sugar matched 34 g<br>blueberry,<br>5: sugar matched 80 g<br>blueberry | Blueberry<br>extended<br>availability of<br>blood glucose in<br>a<br>dose-dependent<br>manner   | [17]      |
| Blueberry | Double-blind,<br>placebo-<br>controlled,<br>parallel study              | overweight and<br>obese<br>participants<br>n = 115<br>(79 M 36 F)<br>age: $63 \pm 7$ y<br>BMI $31.2 \pm 3.0$<br>kg/m <sup>2</sup><br>0 g group $n = 39$<br>13 g group $n = 39$<br>26 g group $n = 37$   | UK      | 6 months   | Freeze-dried<br>blueberry (0 g;<br>13 g; 26 g)   | Participants were<br>instructed to consume<br>1 sachet per day  | Insulin<br>resistance was<br>unaffected   | [20]      |
| Cherry    | NS  | Healthy subjects<br>n = 18 (2 M 16 F)<br>age: 40 $\pm$ 1 y<br>BMI 26.3 $\pm$ 0.9<br>kg/m <sup>2</sup>   | USA     | 28 days<br>intervention<br>followed by 28<br>post-<br>intervention | Sweet cherries<br>280 g/day  | Maintain activity level<br>and diet except to limit<br>the consumption of<br>foods rich in polyphenols<br>and to replace an<br>equivalent amount of<br>dietary carbohydrates<br>with carbohydrates from<br>cherries during the 28 d<br>of cherry consumption.                                   | Supplementation<br>with cherries or<br>cherry products<br>did not alter<br>fasting or<br>randomly<br>sampled BG and<br>FBI in healthy<br>study<br>participants.       | [9]       |
| Cranberry | Single-<br>crossover  | T2DM subjects<br>n = 13 (6  F 7 M)<br>HbA1 c 6.7 ± 0.1%<br>Age: 65.3 ± 1.9 y<br>BMI 34.7 ± 1.6<br>kg/m <sup>2</sup>   | USA     | 4 meal<br>challenges   | Raw<br>Cranberries<br>(RC);<br>White Bread<br>(WB);<br>Sweetened<br>Dried<br>Cranberries<br>(SDC); and SDC<br>with Less<br>added sugar<br>(SDC-LS) | Each subject received<br>4 foods (57 g WB,<br>55 g RC, 40 g SDC,<br>40 g SDC-LC) in random<br>order during a single<br>visit on alternate weeks.  | Plasma insulin<br>for SDC-LS was<br>lower at 60 min<br>than either WB<br>or SDC.<br>Raw cranberries<br>provided the<br>best glycemic<br>and insulinemic<br>responses. | [24]      |

| Fruit     | Study<br>Design          | Study Subjects  | Country | Duration   | Fruit<br>Intervention  | Intervention Diet   | Significant<br>Findings   | Reference |
|-----------|--------------------------|---|---------|--|--|---|---|-----------|
| Cranberry | Randomized,<br>crossover | T2DM<br>overweight<br>subjects $n = 25$<br>(5  M  20  F) age:<br>$56 \pm 6 \text{ y}$ , BMI<br>$39.5 \pm 6.5 \text{ kg/m}^2$<br>Cranberry group<br>n = 12<br>No cranberry<br>group $n = 13$ | USA     | 2 single meal<br>challenges<br>separated by<br>1 week<br>washout | Fast-food-style<br>breakfast (HFB)<br>with or without<br>cranberries   | HFB: 2 scrambled eggs,<br>2 tsp butter, hash brown<br>potatoes (70 g),<br>2 buttermilk biscuits, and<br>a sausage patty (57 g).<br>Cranberry group<br>breakfast: HFB + 40 g<br>dried reduced calorie<br>cranberries<br>No cranberry group:<br>HFB + 80 g ripe banana. | Cranberries<br>intake \ HFB<br>induced PPG<br>and improved<br>selected<br>biomarkers of<br>inflammation<br>and oxidation.<br>Adding whole<br>cranberries to a<br>high-fat meal<br>may improve<br>PPG  | [25]      |
| Mango     | NS                       | Diabetic subject<br>n = 8 age:<br>45-65 y<br>Age-matched<br>healthy subjects<br>n = 6   | India   | Acute<br>consumption   | Fresh mango<br>(50 g) and white<br>bread (14 g)  | After overnight fast, the<br>subjects were given a<br>measured amount of<br>food (white bread and<br>mango) and asked to<br>chew the given quantity<br>of food thoroughly and<br>finish within 10 min; 100<br>mL water was given with<br>each serving.                | management.<br>Mango exerts<br>glycemic<br>response than<br>white bread in<br>both diabetic<br>and non-diabetic<br>individuals.<br>When<br>equi-quantities,<br>mango exerts a<br>significantly<br>glycemic<br>response than<br>white bread in<br>terms of both<br>peak blood<br>glucose (C <sub>max</sub> ) as<br>well as AUC in<br>both diabetic<br>and normal<br>individuals. | [26]      |
| Mango     | Pilot study              | Obese subjects<br>n = 20 (11  M 9 F)<br>age: $36.5 \pm 9.1 \text{ y}$<br>BMI $34.6 \pm 4.0 \text{ kg/m}^2$  | USA     | 10 g FD<br>mango/day   | 12 weeks   | Consume one packet per<br>day (10 g FD mango) in<br>whatever food form they<br>prefer (excluding heating,<br>cooking, or baking). At<br>completion<br>of the 12-week study,<br>subjects underwent their<br>final or post-intervention<br>evaluation.                  | A 12-week<br>dietary<br>supplementation<br>of mango<br>significantly vorall BG in<br>obese<br>individuals.<br>After mango<br>supplementation,<br>insulin levels in<br>males were<br>significantly .<br>Mango<br>supplementation<br>led to no change<br>in glycated<br>hemoglobin or in<br>HOMA-IR.  | [27]      |
| Mango     | Crossover                | Healthy subjects<br>n = 27 (16 M 11 F)<br>age: 26.0 $\pm$ 8.1 y<br>BMI 31.8 $\pm$ 4.1<br>kg/m <sup>2</sup>  | USA     | 12 weeks   | 1 Cup =166 g<br>fresh mango<br>and<br>isocaloric<br>low-fat cookies<br>daily   | During the interventions,<br>participants consumed<br>approximately 100 kcal<br>of<br>fresh mangos (166 g,<br>1 cup, fresh mangos) or<br>low-fat cookies (24 g)<br>daily for 12 weeks<br>separated by 4-week<br>washout.  | Relative to the<br>control snack,<br>mangos may<br>improve certain<br>risk factors<br>associated with<br>overweight and<br>obesity including<br>improved<br>glycemic control<br>and reduced<br>inflammation.  | [28]      |
| Mango     | Randomized,<br>crossover | Healthy subjects<br>n = 24 M age:<br>$21.0 \pm 1.9$ y<br>BMI $24.6 \pm 0.9$<br>kg/m <sup>2</sup>  | USA     | Two one-meal<br>challenges                                       | High-fat meal<br>alone and<br>high-fat meal<br>with the<br>addition of a<br>mango shake<br>(50 g FD mango<br>powder) | After a 10-h overnight<br>fast, consuming a<br>high-fat meal with or<br>without mango shake.<br>The high-fat meal was a<br>typical American<br>breakfast consisting of a<br>sausage and egg biscuit<br>with hash browns from<br>McDonald's.                           | When added to a<br>high-fat meal,<br>acute mango<br>consumption<br>had modest<br>beneficial effects<br>on PPG.  | [29]      |

| Fruit                         | Study<br>Design  | Study Subjects  | Country | Duration   | Fruit<br>Intervention  | Intervention Diet  | Significant<br>Findings   | Reference |
|-------------------------------|--|---|---------|--|--|--|---|-----------|
| Mango                         | Randomized,<br>crossover                                     | overweight and<br>obese subjects<br>n = 23 15 M age:<br>$29.1 \pm 9.5$ y and<br>8 F<br>age: $23.9 \pm 4.3$ y<br>mean BMI 31.3<br>kg/m <sup>2</sup>  | USA     | Two one-day<br>trial   | A 100 kcal fresh<br>mango snack<br>and an<br>isocaloric<br>low-fat cookie<br>snack   | After overnight fast,<br>participants consumed<br>the assigned snacks<br>(fresh mangos (100 kcal)<br>or iso-caloric matched<br>low-fat cookies served<br>with 136 mL of water).<br>Each participant came<br>again for the other snack<br>after 4 weeks.<br>Maintain usual body<br>weight and physical  | The<br>consumption of<br>mangos resulted<br>in ↘ insulin<br>comparatively to<br>low-fat cookies<br>at 45 min post-<br>snack<br>consumption.   | [30]      |
| Mango                         | Single-arm<br>clinical trial                                 | Overweight<br>subjects<br>n = 27 8 M age:<br>$34.6 \pm 7.5$ y<br>BMI $31.21 \pm 1.77$<br>kg/m <sup>2</sup><br>19 F<br>age: $27.0 \pm 6.8$ y<br>BMI $30.03 \pm 3.9$<br>kg/m <sup>2</sup>   | Canada  | 2 cups/day<br>(280 g) of<br>frozen mango   | 8 weeks  | activity level, dietary<br>habits except to consume<br>a maximum of<br>1 serving/day of tea or<br>4 servings/day of coffee;<br>no more than 2 standard<br>alcoholic drinks/week,<br>with red wine being<br>prohibited; and a<br>maximum of<br>2 servings/week of<br>mango-, berry-, or<br>cocoa-containing<br>foods/beverages.<br>Participants were<br>instructed to consume<br>2 cups/day (280 g/day)<br>of frozen mango pulp for<br>8 consecutive weeks. | A ∖ in 2-h<br>plasma glucose<br>concentration of<br>an OGTT is<br>observed after<br>consuming<br>mangos for<br>8 weeks.   | [31]      |
| Mix of<br>berries             | 3<br>randomized<br>controlled<br>trial,<br>crossover         | Healthy females<br>1: $n = 15$ , age:<br>$48 \pm 14$ y, BMI<br>$24.4 \pm 2.7$ kg/m <sup>2</sup><br>2: $n = 13$ , age:<br>$50 \pm 12$ y, BMI<br>$24.2 \pm 3.2$ kg/m <sup>2</sup><br>3: $n = 20$ , age:<br>$47 \pm 12$ y, BMI<br>$24.2 \pm 2.0$ kg/m <sup>2</sup> | Finland | 4 acute<br>consumption<br>tests on<br>separate visits<br>at least 3 days<br>apart. | Berries puree<br>(150 g)<br>1:<br>strawberries,<br>bilberries, or<br>lingonberries<br>2:<br>raspberries,<br>cloudberries, or<br>chokeberries 3:<br>equal amounts<br>of strawberries,<br>bilberries,<br>cranberries, and<br>blackcurrants<br>Cereal bars:<br>Placebo: 0 | The tested meals are:<br>White bread (WB)<br>White bread +150 g<br>whole berry puree<br>Rye bread (RB)<br>Rye bread +150 g whole<br>berry puree  | Strawberries,<br>bilberries,<br>lingonberries,<br>and chokeberries<br>with WB \rangle PPIR.<br>Berry mixture<br>with WB or RB<br>\rangle PPIR.<br>Only<br>strawberries and<br>the berry<br>mixture<br>improved the<br>glycemic profile<br>of WB and RB. | [32]      |
| Raspberry<br>and<br>cranberry | Crossover,<br>randomized,<br>placebo-<br>controlled<br>trial | Healthy subjects<br>n = 20 (18  M  2  F)<br>age: $24 \pm 5 \text{ y}$<br>BMI 26.8 $\pm$ 3.5<br>kg/m <sup>2</sup>  | USA     | 5 acute<br>consumptions<br>separated by<br>at least 5 days                         | freeze-dried<br>(FD) fruit or<br>fruit extract;<br>LOW-Rasp bar:<br>10% FD black<br>raspberries;<br>HIGH-Rasp:<br>20% FD<br>black<br>raspberries;<br>LOW-Cran:<br>0.5%<br>cranberry<br>extract;<br>HIGH-Cran:<br>1.0%<br>cranberry<br>extract.                         | Participants consumed a<br>low-polyphenol diet for<br>two consecutive days<br>before each session and a<br>provided dinner the<br>evening before testing.<br>On test days, participants<br>arrived following a<br>$\geq$ 12 h overnight fast.  | Fortifying a high-<br>carbohydrate bar<br>with a high dose<br>of freeze-dried<br>black raspberry<br>∖ PPI and<br>slowed glucose<br>absorption.  | [33]      |

| Fruit      | Study<br>Design  | Study Subjects  | Country | Duration   | Fruit<br>Intervention   | Intervention Diet  | Significant<br>Findings   | Reference |
|------------|--|---|---------|--|---|--|---|-----------|
| Strawberry | Crossover  | Study 1: healthy<br>subjects $n = 30$<br>(20 F 10 M) age:<br>29.4 $\pm$ 11.7 y<br>BMI 21.6 $\pm$ 2.7<br>kg/m <sup>2</sup><br>Study 2: healthy<br>subjects $n = 8$ M<br>age: 42.4 $\pm$ 4.8 y<br>BMI 23.3 $\pm$ 2.6<br>kg/m <sup>2</sup> | Japan   | Study 1:<br>5 acute<br>consumptions<br>Study 2:<br>7 acute<br>consumptions | Strawberry<br>jams Study 1:<br>Jam S: 24 g Su<br>12.4 g Fr 12.1 g<br>Gl<br>Jam CS: 14.0 g<br>Su 5.7 Fr 14.8 g<br>Gl Jam SG: 16.8<br>Su 7.2 Fr 14.1 g<br>Gl Jam J: 3.4 g<br>Su 24.7 g Fr 14.7<br>Gl 2.4 So Jam<br>PD: 1.6 g Fr<br>1.3 g Gl 2.9 g So<br>Study 2:<br>Strawberry<br>jams (SG, J and<br>MT: low-calorie<br>strawberry jam<br>with malitol) | Study 1: Each subject<br>took the 5 strawberry<br>jams (S, CS, SG, J, PD) on<br>separate mornings.<br>Participants arrived<br>following a $\geq$ 12 h<br>overnight fast. Nothing<br>was allowed to be eaten<br>or drunk except water.<br>All subjects took a 50 g<br>carbohydrate load of<br>reference food (glucose:<br>50 g) and the test meal.<br>Study 2: test meals are<br>only 20 g jam (SG, J, MT);<br>only one slice of bread<br>(60 g); or one slice of<br>bread with 20 g jam. | Study 1: The BG<br>level for jam S<br>and jam J were<br>lower than the<br>reference glucose<br>level at several<br>points.<br>Study 2: Eating<br>one slice of bread<br>(60 g) with less<br>than 20 g of<br>strawberry jam<br>had no influence<br>on the PPG level<br>or the AUC | [34]      |
| Strawberry | Crossover,<br>placebo-<br>controlled,<br>single-blind,<br>randomized,<br>single-center                             | Overweight<br>subjects $n = 26$<br>(10 M 16 F) age:<br>$50.9 \pm 15.0$ y<br>BMI 29.2 $\pm 2.3$<br>kg/m <sup>2</sup>   | USA     | 2 meal<br>challenges   | Strawberry<br>beverage and<br>strawberry<br>flavored<br>beverage as<br>placebo  | A 7-day run-in period<br>avoiding consumption of<br>berries, while<br>maintaining all other<br>aspects of the diet and<br>physical activity.<br>Test meal: Bagel (110 g),<br>cream cheese (14 g),<br>margarine (5 g),<br>hard-boiled egg (50 g),<br>cantaloupe (85 g) whole<br>milk (240 g), and<br>strawberry or placebo<br>beverage (305 g)  | The strawberry<br>beverage $\searrow$<br>postprandial<br>inflammatory<br>response (CRP<br>and IL-6).<br>The strawberry<br>beverage $\searrow$<br>PPIR.  | [35]      |
| Strawberry | Randomized,<br>crossover,<br>double-blind<br>with three<br>arms  | Healthy subjects<br>n = 16 (6 M 10 F)<br>age: 25.94 $\pm$ 3.02 y<br>BMI 23.99 $\pm$ 3.05<br>kg/m <sup>2</sup>   | Spain   | Acute<br>consumption<br>at days 0, 7,<br>and 14                            | 3 Strawberry<br>jams<br>HS (high added<br>sugar) with LS<br>(low sugar<br>naturally<br>occurring)<br>LSA (low sugar<br>naturally<br>occurring with<br>added<br>strawberry<br>pulp extract)  | Maintaining the physical<br>activity and habitual diet<br>while avoiding<br>antioxidant-rich food<br>products the week before<br>to test the meals. 3 nights<br>before the intervention<br>consume a standardized<br>dinner and arrive after<br>10 h fasting.<br>The participants<br>subsequently received<br>60 g of jams HS, LS, or<br>LSA in a randomized<br>order in days 0, 7, and 14.  | For low-sugar<br>jams, BG<br>remained at<br>normal values<br>and without<br>peaks within 2 h.<br>BG and BI were<br>higher at 30 and<br>60 min after<br>high-sugar (HS)<br>jam intake<br>versus both<br>low-sugar jams.  | [36]      |
| Strawberry | Randomized<br>control trial,<br>crossover,<br>4-arm,<br>single-center,<br>single-<br>blinded,<br>dose-<br>response | Obese insulin<br>resistant subjects<br>n = 21 (5 M 16 F)<br>age: $39.8 \pm 13.8$ y<br>BMI 40.2 $\pm$ 7.2<br>kg/m <sup>2</sup>   | USA     | Four separate<br>6 h<br>postprandial<br>visits                             | Strawberry<br>freeze-dried<br>(FD) milk-based<br>beverages (0, 10,<br>20, or<br>40 g FD<br>strawberry<br>powder)  | activity and habitual diet<br>while limiting all berry<br>products during the<br>study and<br>polyphenolic-containing<br>foods 3 days prior to<br>each visit.<br>Visits were no less than<br>3 d and no more than<br>14 d apart.<br>Standard meal: a bagel<br>with cream cheese and<br>margarine, a hard-boiled<br>egg, cantaloupe, and<br>whole milk.   | The 40 g FD<br>strawberry<br>beverage \ PPI<br>over 6 h.<br>Strawberry<br>intake insulin<br>demand to<br>manage PPG in<br>obese<br>individuals with<br>insulin<br>resistance.   | [37]      |

| Fruit  | Study<br>Design   | Study Subjects   | Country | Duration   | Fruit<br>Intervention   | Intervention Diet   | Significant<br>Findings   | Reference |
|--|---|--|---------|--|---|---|---|-----------|
| Strawberry<br>and extract<br>of<br>cranberry | Double-blind,<br>parallel,<br>randomized<br>control trial | Overweight or<br>obese and<br>insulin-<br>resistant subjects<br>Strawberry and<br>cranberry group<br>n = 20 (9  M 11 F)<br>age: 57 ± 1 y<br>BMI 31 ± 1 kg/m <sup>2</sup><br>Control group $n$<br>= 21 (12 F 9 M)<br>age 60 ± 1 y BMI<br>31 ± 1 kg/m <sup>2</sup> | Canada  | 6 weeks  | 120 mL/day of<br>beverage:<br>Strawberry<br>and cranberry<br>beverage (SCP):<br>1.84 g mixture<br>of dry<br>strawberry and<br>cranberry<br>polyphenol<br>extract Placebo:<br>strawberry<br>flavored | Maintain usual food<br>habits and physical<br>activity level; limited to<br>one unit drink or less of<br>beer or spirits per day<br>and no consumption of<br>berries, wine,<br>polyphenol.<br>Supplements, and all<br>products containing<br>berries or wine.<br>Participants in the<br>treatment group<br>consumed one SCP<br>beverage whereas the<br>Control group received a<br>flavor-matched SCP-free<br>Control beverage, daily<br>for a 6-week period. | 6-week<br>consumption of<br>333 mg<br>polyphenols<br>from<br>strawberries and<br>cranberries may<br>improve insulin<br>sensitivity and<br>prevent an<br>increase in<br>compensatory<br>insulin secretion<br>without affecting<br>plasma lipids,<br>CRP, pro-<br>inflammatory<br>cytokines and<br>antioxidant<br>capacity. | [38]      |
| Watermelon                                   | Crossover   | Overweight and<br>obese adults<br>n = 33 (20  M  13  F)<br>age: 18–55 y BMI<br>$30.5 \pm 3.5 \text{ kg/m}^2$   | USA     | two 4-week<br>interventions<br>separated by a<br>2–4-week<br>washout<br>period | 2 cups of fresh<br>watermelon (92<br>kcal) or<br>isocaloric-<br>matched<br>low-fat cookies<br>as snacks   | Maintaining their typical<br>dietary intakes and<br>physical activity levels,<br>participants could<br>consume their snacks at<br>any time of day, during<br>one or multiple sittings,<br>alone or in combination<br>with other foods.<br>They were asked to<br>avoid consuming low-fat<br>cookies during the<br>watermelon intervention<br>and to avoid consuming<br>watermelon during the<br>low-fat cookies'<br>intervention.                              | Following the<br>four-week<br>interventions,<br>serum glucose<br>levels were not<br>significantly<br>different<br>between the<br>watermelon and<br>low- fat cookies<br>interventions.<br>There were no<br>significant<br>changes in<br>serum glucose<br>between baseline<br>and week four<br>within each<br>intervention. | [39]      |
| Watermelon                                   | Randomized<br>2-arm design                                | Overweight and<br>obese<br>postmenopausal<br>women<br>Control group<br>n = 19 age:<br>$60.1 \pm 1.6$ y BMI<br>$30.3 \pm 1.1$ kg/m <sup>2</sup><br>Watermelon<br>group $n = 26$ age:<br>$59.5 \pm 1.0$ y BMI<br>$30.9 \pm 0.9$ kg/m <sup>2</sup>                  | USA     | 6 weeks  | Watermelon<br>puree (710 mL)  | The watermelon group<br>consumed 710 mL of<br>watermelon puree per<br>day whereas the control<br>group consumed no<br>watermelon. Each<br>participant completed a<br>$\pm$ 9-h overnight fast<br>prior to the pre- and<br>post-visits of the 6-week<br>study period.  | Within the<br>watermelon<br>group, FBC, FBI,<br>and HOMA-IR<br>did not change<br>during the study<br>period and<br>similarly in the<br>control group.<br>The pattern of<br>change of<br>estimated insulin<br>resistance did<br>not differ<br>between groups.  | [40]      |

Table 1. Cont.

Although Hameed et al. [16] have previously provided a review on this topic, further research investigating the impacts of different forms of blueberry consumption on glucose homeostasis in adults with T2DM would greatly benefit our current understanding of this relationship, especially given that blueberries have low glycemic index (GI) and medium glycemic load (GL) (Table 2). Existing evidence suggests that people with diabetes may consume blueberries in any form without negative health effects. Nonetheless, longer and larger-scale clinical trials focusing on male and female T2DM patients of various ages, as well as nutrition timing (pre- vs. post-prandial glucose levels) and optimum/maximum amount of blueberry consumption, need to be conducted to conclude that blueberry consumption does not impair blood glucose homeostasis.

| Fruit                        | Form  | Glycemic Index                 | Serving Size | Glycemic Load<br>(per Serving) | Reference |
|------------------------------|-------|--------------------------------|--------------|--------------------------------|-----------|
| Apples                       | Raw   | $38\pm2$                       | 120 g        | 6                              | [41]      |
| Blueberries                  | Raw   | 53                             | 1 cup        | 12                             | [41]      |
| Cherries                     | Raw   | 22                             | 120 g        | 3                              | [41,42]   |
| Cranberries                  | Juice | $56 \pm 4$                     | 250 mL       | 16                             | [41]      |
| Dates (depending on variety) | Dried | 42.8 $\pm$ 5.5 to 103 $\pm$ 21 | 60 g         | 8.5–9.2 to 42                  | [41,43]   |
| Mangoes                      | Raw   | $51\pm5$                       | 120 g        | 8                              | [41]      |
| Orange                       | Juice | $52 \pm 3$                     | 250 mL       | 15                             | [41]      |
| Raisins                      | Dried | $64\pm11$                      | 60 g         | 25                             | [41]      |
| Strawberries                 | Raw   | $40\pm7$                       | 120 g        | 4                              | [41]      |
| Strawberries                 | Jam   | $51\pm10$                      | 30 g         | 10                             | [41]      |
| Watermelon                   | Raw   | $72\pm13$                      | 120 g        | 4                              | [41]      |

**Table 2.** Summary of glycemic index and glycemic loads of the studied whole fruits, dried fruits, and fruit juices.

# 3.1.2. Cranberries

Cranberries are berries rich in a variety of nutrients and phytochemicals including but not limited to phenolic acids, anthocyanins, flavones, flavonoids, and organic acids [44]. To the best of our knowledge, there are only two clinical trials that examined the effects of cranberry consumption on glycemic responses in individuals with T2DM (Table 1). However, both studies examined the acute effects on glucose homeostasis, as they dealt with meal challenges with/without cranberries. Compared to white bread and sweetened dried cranberries, the acute consumption of raw cranberries and minimally sweetened dried cranberries resulted in a negligible increase in plasma glucose and insulin levels [24]. In another study comprising overweight T2DM participants, the acute consumption of dried cranberries following a high-fat breakfast resulted in a significantly lower postprandial glucose increase compared to the control group (no cranberries) and improved certain inflammation and oxidative biomarkers, namely IL-18 and malondialdehyde [25]. This suggests that adding whole cranberries to a high-fat meal may positively affect postprandial blood glucose levels. Future clinical trials should be conducted to examine the long-term effects of cranberry consumption on hemoglobin A1C (Hb1AC) levels, which reflects an average blood glucose level over a time period of three months. Further, it would be of interest to determine GI and GL of different forms of cranberries.

#### 3.1.3. Strawberries

Strawberries are one of the most consumed fruits worldwide, either in its whole form or as one of its derivatives (e.g., juice, jelly, and jam). Similar to blueberries, strawberries are also rich in anthocyanin. Park et al. [37] and Edirisinghe et al. [45] studies investigated the effects of strawberry intake on insulin homeostasis. In one study assessing the acute effects of consuming beverages containing freeze-dried whole strawberry powder with a high-carbohydrate, high-fat meal in obese adults with insulin resistance, the authors found that compared to the placebo group, participants had significantly reduced post-prandial insulin concentrations after 6 h [37]. The studies conducted by Rohm et al. [46] and Matsumori et al. [35] have also demonstrated the associations between chronic low-grade inflammation and the pathogenesis of T2DM. In the study conducted by Edirisinghe et al. [45], it was reported that strawberry consumption reduced inflammatory biomarkers, suggesting that strawberry consumption may result in improved glucose homeostasis (Table 1). Focusing on overweight adults, the authors reported that the consumption of high-fat breakfasts with beverages containing freeze-dried whole strawberry powder significantly decreased their postprandial inflammatory response, as evidenced by reduced C-reactive protein (CRP) and interleukin-6 (IL-6) levels [45]. It has been proposed that the ingestion of a high-fat meal may serve as a stimulus to raise systemic inflammatory response [47].

When strawberries are produced and consumed as jams, we need to also consider the amount and type of sweeteners used during the preparation, which may modify the GI and GL of the obtained food products (Table 2). Various studies in the past used strawberry jam containing added sugar or other sweeteners to investigate the effects of strawberry consumption on parameters of blood glucose homeostasis. A study by Ibero-Baraibar et al. found that the acute intake of low-sugar strawberry jam in healthy subjects did not alter normal blood glucose levels for the first two hours after consumption. Conversely, researchers found that the acute consumption of high-sugar strawberry jam spiked their blood glucose and insulin levels at 30 min and 60 min timepoints post-ingestion [36]. Kurotobi et al. found that when using strawberry jam prepared with various sugar compositions, the blood glucose of healthy participants was lower than the reference glucose level at several time points [34]. A separate study conducted by the same authors found that ingesting one slice of bread (60 g) with less than 20 g of strawberry jam had no influence on the postprandial glucose level or area under the curve. These pieces of evidence suggest that strawberries can be part of a healthy diet for individuals with T2DM.

#### 3.1.4. Acai Berries

Many studies have examined the effects of acai berries, including their anti-inflammatory and antioxidative properties, to determine their influence on various health outcomes as reported in the review conducted by Hameed et al. [16]. However, most of these studies are conducted in animals. To the best of our knowledge, there is only one pilot study assessing the effects of acai berries consumption on health parameters in humans [21] (Table 1). This pilot study prompted overweight participants to consume smoothies prepared with acai pulp for four weeks. At the end of the study, the authors found that their fasting glucose and insulin levels were significantly reduced compared to baseline. More human model research on this fruit needs to be conducted so that its effects on glucose homeostasis can be determined. Besides, it would be of interest to evaluate the GI and GL of berries, which will help understand their effects on glucose homeostasis.

#### 3.1.5. Mix of Berries

Since snacking on berries in an assorted variety is an extremely popular form of consumption, we hereafter present the clinical studies that have chosen to use mixed berries as their study intervention (Table 1). Paquette and colleagues investigated the effects of consuming beverages prepared from a mix of strawberries and cranberries in overweight or obese participants with insulin resistance for 6 weeks and found that the treatment improved insulin sensitivity and prevented an increase in compensatory insulin secretion without affecting plasma lipids, CRP, pro-inflammatory cytokines, and antioxidant capacity [38]. In another study where healthy young subjects participated in an acute consumption tests of high-carbohydrate cereal bars fortified with raspberries and cranberries, the investigators found that adding black raspberries to the bars slowed down their glucose absorption and decreased their postprandial levels [33]. A study by Törrönen et al. used other berry mixes (strawberries, bilberries, lingonberries, raspberries, cloudberries, chokeberries, cranberries, and blackcurrant) and found that all berries independently or in mixture improved the glycemic parameters in middle-aged females. The berry mixture containing equal amounts of strawberries, bilberries, cranberries, and blackcurrant when eaten with white or rye bread decreased the postprandial insulin response [32]. Data from these studies collectively suggest that the consumption of all berries may not be harmful to individuals with T2DM. Future studies should focus on examining the effects of mixed berries consumption on HbA1c levels and long-term effects on glycemic control before they can be safely recommended to T2DM patients.

## 3.1.6. Apples

Apples are among the most consumed fresh fruits worldwide. Though there are more than 7500 varieties of apples in the world, the top five apples that are produced in

the U.S. are namely Red Delicious, Gala, Granny Smith, Fuji, and Golden Delicious [48]. Different varieties of apples have similar nutrient compositions, thus offering similar health benefits [49]. Apples have a relatively low glycemic index (GI = 36), and they contain a high amount of dietary fiber including pectin, which is a soluble fiber (Table 2) [42]. Nonetheless, it should be noted that pectin in apples degrades as the apples ripen, losing its potency as it breaks down into smaller molecules [50]. Inoue et al. [22] compared the effects of apple intake in both healthy participants and participants with impaired glucose. These apples were consumed once before white rice and on another occasion after white rice. It emerged that apple consumption before meals could improve postprandial hyperglycemia in both groups. In another study by Lu et al., the investigators compared the effects of apple, pear, and orange consumption as preloads to white rice meals among healthy young individuals (Table 1). The results from the study indicated that all preloaded treatments resulted in a significant reduction (p < 0.001) of incremental peak glucose (IPG) and the maximum amplitude of glycemic excursion in 180 min, as well as a significant decrease (p < 0.05) in postprandial glycemic response [23]. Despite these positive findings, future studies in individuals with prediabetes and T2DM need to be conducted to determine the long-term effects of apple consumption in these populations.

#### 3.1.7. Watermelon

Watermelon is known as one of the richest fruit sources of lycopene (48.7 mg/kg of fresh weight) and is also high in citrulline and many other beneficial compounds [51]. Lycopene and citrulline have been associated with decreased incidence of prostate cancer and improved cardiovascular health, respectively [52,53]. Additionally, evidence suggests that watermelon consumption may not impair glucose homeostasis (Table 1). In a recent clinical study investigating the effects of watermelon consumption in overweight and obese adults for 4 weeks, the investigators found no significant difference in serum glucose levels from baseline [39]. Similar results were observed in another interventional study conducted in overweight and obese postmenopausal women for 6 weeks. In the study, no significant changes were observed in fasting blood glucose, fasting blood insulin, and HOMA-IR at the end of study period in both treatment and control groups [40]. Nonetheless, individuals with T2DM should be mindful of the portion of watermelon they consume owing to its high GI (Table 2), as well as when they consume it (pre- or post-meals and/or as snack).

### 3.1.8. Cherries

Cherries are one of the most studied fruits in the world as they are rich in polyphenols, particularly anthocyanins [54]. In a study by Kelley et al., a group of middle-aged healthy participants were asked to consume cherries daily for 28 days (Table 1). Post intervention, the investigators did not observe any significant changes in their fasting blood glucose and fasting blood insulin levels [9]. These unaltered levels may be due to cherry's naturally very low glycemic index (Table 2). Nonetheless, research suggests that individuals with T2DM may benefit the most from consuming cherries in moderation.

#### 3.1.9. Mangoes

The latest study by Zarasvand et al. [55] presented an extensive review of the studies conducted on mangoes (leaves, flesh, and seeds) for their various health benefits using cell cultures, in vitro and in vivo methods, as well as clinical trials. Mangiferin is the compound most studied from the mango plant, which gives mangoes their antidiabetic properties [56]. Several studies have investigated mangoes intake by a variety of participants (Table 1). Supplementing a high-fat, fast-food-type breakfast for healthy young subjects with mangoes showed a modest beneficial effect on their postprandial glucose levels [29]. In another 12-week intervention study among healthy young subjects, consuming fresh mangos compared to low-fat cookie snacks, investigators observed an improvement in glycemic control and a reduction in inflammation levels in the group consuming fresh mangoes [28]. In one pilot study, obese subjects were recruited and asked to consume

mangoes for 12 weeks. Here, the authors reported a decrease in blood glucose levels, no change in glycated hemoglobin or in HOMA-IR, and an increase of insulin levels (only in male participants) [27]. After daily consumption of frozen mangoes by overweight participants for 8 weeks, a significant reduction in 2 h plasma glucose of an oral glucose tolerance test was observed compared to baseline [31]. In another study, an acute consumption of mangoes by overweight and obese subjects led to a decrease in insulin levels compared to low-fat cookies at 45 min post intake [30]. Only one study focused on diabetic subjects and reported that fresh mango intake led to a decrease in glycemic response in terms of peak blood glucose and area under curve compared to white bread both in healthy individuals and individuals with T2DM [26]. Current evidence suggests that moderate mango consumption, in regard to its GI and GL (Table 2), would be considered safe for individuals with T2DM.

## 3.2. Dried Fruit

Dried fruits have long been considered a healthy snack option due to their high nutrient content, including vitamins, minerals, and fiber. However, for individuals with T2DM, the impact of consuming dried fruit on blood sugar levels and overall health may be a concern. While dried fruit can offer many health benefits, including potentially reducing the risk of developing T2DM, their high sugar and calorie content reflecting their GI and GL can also lead to negative health outcomes if consumed in excess (Table 2). Therefore, understanding the relationship between dried fruit and T2DM is important for individuals with this condition especially when it is evidence-based by clinical trials (Table 3) to make informed decisions about their dietary choices.

#### 3.2.1. Raisins

Raisins are widely consumed throughout the world; the raisin market was valued at USD 2404.75 million in 2022 and is projected to reach USD 3590 million by 2030 [57]. Several studies have demonstrated beneficial effects of grape polyphenols, e.g., anthocyanins and resveratrol present in the seeds. Most of these studies have used seeds or other derivatives of grapes such as wine, juice, and pomace. However, realistically speaking, most consumers do not eat the seeds and prefer varieties of grapes that are seedless. Despite the number and variety of phytochemicals identified in grapes, to our knowledge no studies have focused on the impact of fresh grapes intake in a diabetic population.

On the other hand, there are several studies that have used raisins and have demonstrated positive health benefits for individuals with T2DM [9-63]. Raisins are rich in various dietary components such as dietary fiber, which varies depending on the variety of grapes used. Raisins are also rich in micronutrients such as potassium, zinc, copper, and selenium. Raisins are also high in vitamin C, thiamin, and riboflavin, which play important roles in regulating glucose homeostasis [59]. A study by Sebastian et al. compared acute consumption of raisins between healthy and T2DM participants and showed that raisins decreased glucose and insulin responses in both groups [60]. Snacks make up nearly one-quarter of daily energy consumed by adults in the U.S. [61]. A study conducted by Anderson et al. [62] in participants with prehypertension and mild hyperglycemia consuming raisins or low-fat snacks for 12 weeks highlighted at the end of the study period a decrease of postprandial glucose (13.1 mg/dL) and a significant (p = 0.004) reduction in HbA1c value within the raisin group. A similar study was conducted in T2DM participants and similar results were observed, where the group consuming raisins had a decrease in postprandial glucose (p = 0.033) and fasting blood glucose by 13.5 mg/dL (p = 0.09) [63]. However, the decrease in HbA1c was not significant (p = 0.173). Altogether, the data suggest that raisins could be consumed by individuals with T2DM, which may help in improving their glycemic response.

# 3.2.2. Dates

Dates are and have been one of the most important fruits in the Middle East, North Africa, and Arabian Peninsula for centuries. Depending on the area of farming and species of date palm, their nutrient contents vary from one to another [64]. Despite the variation, nutritional analysis shows that dates contain mainly carbohydrates and sugar (70%) in the forms of glucose, fructose, and a small amount of sucrose. A review by Mirghani [43] compared the glycemic index of different date varieties from different countries by examining several studies. It appears that most date varieties have glycemic indexes that are not significantly different from each other while Foster-Powell et al. [41] reported a different GI (Table 2). Five varieties of dates were investigated by Alkaabi et al. [65]. The results showed that T2DM individuals who consumed these varieties exhibited no impact in significant postprandial glucose excursions. Dates also contain fibers, vitamins, and minerals in consequent amounts, as well as a large range of nutrients such as calcium, magnesium, amino acids, iron, zinc, potassium, phosphorus, and selenium [66,67]. Along with these nutrients, some non-nutrient phytochemicals with biological activities were reported in the dates, e.g., carotenoids, polyphenols, phenolic acids [68,69]. These bioactive compounds were identified as able to decrease the postprandial hyperglycemia for T2DM individuals [70]. For a more comprehensive understanding of dates' composition and their effects on a variety of metabolic variables, please refer to the latest review by Meenakshi and Misla [71].

Investigating the impact of date consumption on glucose homeostasis for T2DM is of high interest. Indeed, Rock et al. reported findings from T2DM participants who consumed three dates daily for 16 weeks that showed no increase of their HbA1c levels [72]. This result corroborates that fructose is less rapidly absorbed than glucose [73]. Moreover, the daily intake of dates did not affect the participant's BMI or lipid profile. In a recent 2022 study conducted by Al-Msallem et al. [74] on individuals with T2DM where the researchers compared the effects of various servings of dates consumption daily (<1, 1–3, >3 servings per day), a decrease in HbA1c was reported independently of the number of dates consumed. Indeed, the regular consumption of dates did not affect T2D patients' glycemic control, and surprisingly, patients consuming many dates had significantly lower HbA1c than those who consumed few of them (p < 0.05). Furthermore, the association between HbA1c level and the number of dates consumed remained statistically significant after adjustment for BMI, treatment type, and consumption of fruits and vegetables, breads, grains, and confectionary. In another study, with T2DM participants, the researchers compared dates and a glycemic-matched control consumption for 12 weeks. It appeared that consumption of 60 g of dates daily had no deleterious impact on glycemic control nor any cardiometabolic risk parameter [75].

Therefore, it is justified to state that regular dates consumption helps regulate plasma glucose concentration by improving HbA1c and blood glucose levels despite their high fructose content. These findings suggest that individuals with T2DM may include dates in a moderate amount as part of their diets to meet their fruits intake recommendation.

Table 3. A summary of clinical studies examining glycemic index and the intake of dried fruits.

| Fruit | Study Design | Study Subjects  | Place | Duration             | Fruit<br>Intervention  | Intervention Diet   | Significant Findings   | Reference |
|-------|--------------|---|-------|----------------------|--|---|--|-----------|
| Dates | NS           | T2DM patients $n = 10$<br>(5 M 5 F)<br>age: 40.8 ± 5.7 y<br>BMI 30.7 ± 5.2 kg/m <sup>2</sup><br>Healthy participants<br>n = 13 (6 M 7 F)<br>age: 40.2 ± 6.7 y<br>BMI 27.4 ± 4.1 kg/m <sup>2</sup> | UAE   | Acute<br>consumption | 50 g equivalent<br>carbohydrate<br>of varieties<br>Fara'd, Lulu,<br>Bo ma'an,<br>Dabbas, and<br>Khalas, and<br>50 g of glucose | Glycemic index<br>evaluation:<br>50 g of glucose and<br>5 varieties of dates<br>with 250 mL | The tested varieties of<br>dates have low GIs in<br>healthy subjects.<br>Consumption of the<br>tested varieties of dates<br>by diabetic individuals<br>does not result in<br>significant postprandial<br>glucose excursions. | [65]      |

| Fruit   | Study Design   | Study Subjects  | Place            | Duration  | Fruit<br>Intervention   | Intervention Diet   | Significant Findings  | Referenc |
|---------|--|---|------------------|---|---|---|---|----------|
| Dates   | Cross-<br>sectional<br>observational<br>study                          | T2DM patients<br>n = 404 (207 M 197 F)<br>BMI: <18.5 kg/m <sup>2</sup> :<br>n = 1;<br>18.5 < BMI < 25<br>kg/m <sup>2</sup> : $n = 20;$<br>25 < BMI < 30<br>kg/m <sup>2</sup> : $n = 92;$<br>30 < BMI < 35<br>kg/m <sup>2</sup> : $n = 226;$<br>BMI > 35 kg/m <sup>2</sup> :<br>n = 65 | Saudia<br>Arabia |   | Dates serving<br>size<br><1: (0–26 g)<br>equivalent to<br>3 pieces<br>1–3 servings:<br>(27–81 g)<br>>3 servings:<br>(>81 g)   | Frequency of<br>consumption<br>assessed by<br>validated<br>questionnaire  | High consumption of<br>date fruits was<br>statistically significantly<br>correlated with lower<br>HbA1 c and fasting<br>blood glucose in<br>patients with T2DM.   | [74]     |
| Dates   | Randomized<br>controlled trial   | T2DM patients<br>n = 46 age:<br>$55.25 \pm 2.71$ y<br>BMI 28.45 $\pm$ 7.69<br>kg/m <sup>2</sup><br>Healthy participants<br>n = 50 age:<br>$56.86 \pm 4.41$ y<br>BMI 29.92 $\pm$ 4.11<br>kg/m <sup>2</sup>   | Bahrain          | 16 weeks  | 3 dates daily as<br>part of<br>breakfast  | The participants<br>were instructed to<br>consume 3 dates<br>daily as part of<br>their breakfast with<br>no change in their<br>habitual diet  | The daily low intake of<br>dates in T2DM subjects<br>did not increase HbA1 c<br>levels.<br>Daily dates<br>consumption could<br>have a beneficial effect<br>on lipid profile by<br>reducing total<br>cholesterol and<br>elevating HDL.   | [72]     |
| Dates   | Randomized controlled trial  | T2DM participants<br>Date group $n = 39$<br>(21 M 18 F)<br>age: 61 ± 10 y BMI<br>31.3 ± 6.2 kg/m <sup>2</sup><br>Raisin group $n = 40$<br>(18 M 22 F)<br>age: 56 ± 9 y BMI<br>31.3 ± 5.7 kg/m <sup>2</sup>  | Bahrain          | 12 weeks  | Dates groups:<br>60 g Raisins<br>group: 60 g  | The dried fruits<br>were consumed<br>twice daily at<br>midmorning and<br>midafternoon.  | Consumption of dates<br>at an acceptable level<br>for Middle Eastern<br>country (60 g) daily by<br>T2DM individuals had<br>no effect on glycemic<br>control nor any<br>cardiovascular risk<br>parameters.   | [75]     |
| Raisins | Randomized,<br>crossover   | Healthy subjects<br>n = 15 (8  M 7 F)  age:<br>$25.9 \pm 0.8 \text{ y BMI}$<br>$21.3 \pm 0.3 \text{ kg/m}^2$<br>Diabetic subjects<br>n = 15 (9  M 6 F)<br>age: $63.2 \pm 1.7 \text{ y}$<br>BMI $31.5 \pm 1.3 \text{ kg/m}^2$  | Greece           | Two one- day<br>trial separated<br>by 3 days<br>minimum | 50 g of glucose<br>diluted in glass<br>of water or 74 g<br>portion of<br>Corinthian<br>raisins  | After overnight<br>(10–12 h) fasting,<br>the subjects<br>consumed either<br>50 g of glucose<br>diluted in a glass of<br>water or a 74 g<br>portion of<br>Corinthian raisins.<br>Subjects were<br>instructed to chew<br>the raisins very<br>well prior to<br>swallowing. | Corinthian raisins<br>consumption \sqrt{glucose}<br>and insulin responses in<br>healthy and diabetic<br>subjects, compared to<br>reference.<br>In diabetics,<br>postprandial response<br>indicated \sqrt{in}<br>absorption rates as the<br>absorption of sugars<br>declines in older age.             | [60]     |
| Raisins | Randomized<br>controlled trial   | patients with<br>prehypertension and<br>mild hyperglycemia<br>Snacks group $n = 15$<br>(9 M 6 F) age: 61.1 y<br>BMI 29.2 $\pm$ 0.6 kg/m <sup>2</sup><br>Raisins group $n = 31$<br>(12 M 19 F)<br>age: 60.3 y BMI<br>30.0 $\pm$ 0.5 kg/m <sup>2</sup>                                  | USA              | 12 weeks  | 28 g of<br>prepacked dark<br>dry Californian<br>raisin and<br>comparable<br>snacks non<br>containing<br>raisins or<br>predominantly<br>fruits or<br>vegetables and<br>not over 10 g of<br>sugar per<br>serving 3<br>times/day | Both raisins and<br>snacks were to be<br>eaten 3 times daily<br>with 8-oz of a<br>non-caloric<br>beverage<br>(preferably water<br>but non-caloric soft<br>drinks or a hot<br>beverage were<br>acceptable).  | FPG levels were not<br>affected by intake of<br>raisins or snacks.<br>Mean subject PPG were<br>significantly ∖ by<br>raisin intake at 12<br>weeks.<br>Eating raisins<br>significantly ∖ HbA1 c,<br>greater than the<br>decrease seen with<br>snack intake.  | [62]     |
| Raisins | Unblinded,<br>single-site,<br>active<br>randomized<br>controlled trial | T2DM patients with<br>inadequate glycemic<br>Control group $n = 19$<br>(9 M 10 F)<br>age: 59 y BMI 34 $\pm$ 5<br>kg/m <sup>2</sup> Raisin group<br>n = 27 (10 M 17 F)<br>age: 58 y BMI 37 $\pm$ 7<br>kg/m <sup>2</sup>  | USA              | 12 weeks  | 28 g of<br>prepacked dark<br>dry Californian<br>raisin and<br>comparable<br>snacks non<br>containing<br>raisins or<br>predominantly<br>fruits or<br>vegetables and<br>not over 10 g of<br>sugar per<br>serving<br>3 times/day | The participants<br>were instructed to<br>consume the<br>allocated snacks<br>3 times per day<br>with 8-oz of<br>non-caloric soft<br>drinks or hot<br>beverage   | For T2DM patients<br>compared to alternative<br>processed snacks, those<br>who consumed raisins<br>had significantly<br>PPG to a statistical and<br>clinically relevant<br>degree.<br>Compared to snacks,<br>those who consumed<br>raisins had<br>HbA1c, although not to<br>statistical significance. | [63]     |

BMI: body mass index; FBG: fasting blood glucose; FPG: fasting plasma glucose; GI: glycemic index; HbA1c: hemoglobin A1C; HDL: high-density lipoprotein; NS: not specified; PPG: postprandial glucose; S: decrease.

In 2022, the average consumption of fruit juices measured 17.7 L out of 422.16 L per capita of nonalcoholic beverages for the U.S. These beverages were bottled water, ready-to-drink coffee and tea, soft drinks, and juices [76]. Therefore, several clinical studies investigated the impact of some fruit juices intake on glucose metabolism of different consumers (Table 4).

#### 3.3.1. Cranberry Juice

Due to their richness in phytochemicals ensuring great health benefits for humans, cranberries are consumed in a variety of forms: fresh, dried, sweetened dried, and juices [44]. A cross-sectional study compared the impact of different forms of cranberry juice consumption in a group of young healthy participants. It appeared that consumption of unsweetened cranberry juice is associated with a favorable glycemic response [77]. Building on these findings, daily intake of low-calorie cranberry juice for 8 weeks by middle-aged participants highlighted a decrease in fasting plasma glucose [78]. When studied in a T2DM population, regular cranberry juice consumption for 12 weeks showed a decrease in serum glucose [79]. Therefore, since regular cranberry juice is shown to benefit individuals with T2DM despite its medium GI and high GL (Table 2), the authors suggest that cranberry could be consumed by individuals with T2DM, especially in its fresh or unsweetened forms in a moderate amount.

#### 3.3.2. Orange Juice

One of the most widely consumed and beloved beverages is orange juice. The global consumption of fruit beverages reached 95.69 billion liters in 2018. Of this total volume, juice 'drink' accounted for 37.23 billion liters, making it the largest subcategory consumed. Juice 'drink' subcategory is closely followed by nectar, (100% juice) and powdered or concentrated juice out of the consumed fruit beverages. Among the flavors most preferred by consumers in 100% juice category, orange is the clear favorite, representing 43.8% of the market. In the nectar category, orange takes the first position again accounting for 18.9% of consumption. In the juice drinks segment, orange flavor also occupies the first position with 26.2% of the market [80]. Some follow-up studies focused on the impact of orange juice and the incidence of these juices' consumption on T2DM (Table 4). The intake of fruit juices was found to be positively associated with T2DM incidence among a female population of 71,346 participants that were followed for 18 years [81]. In fact, consuming more than 1 cup of orange juice increases this risk by 24%, compared to individuals who get less than 1 cup. When the studied cohort was extended to three prospective longitudinal cohort studies, the researchers concluded that replacing fruit juices with fresh oranges reduces the risk of T2DM by 8%, while consuming one serving per day of apple, orange, or grapefruit juice increases that risk by 21% compared to the people who did not consume juice [82].

Focusing on healthy subjects' consumption of orange juice, it appeared that daily intake of 300 mL of orange juice by healthy young females significantly reduced fasting blood glucose, postprandial insulin, and HOMA-IR after 60 days of intervention. The participants in this study underwent a washout period of 30 days and all the reduced levels went back to their initial value before orange juice consumption [83]. Similar results were found by Lima et al., which reported a significant decrease in blood glucose insulin and HOMA-IR index [84]. In another study, regarding when orange juice is consumed, young healthy participants were invited to have orange juice during two separate periods, with the meals or between meals. The results obtained showed an increase in fat mass and a decrease in postprandial insulin sensitivity after between meals intervention. By contrast, after consumption in the between meals group, fat mass and gamma-glutamyl transferase decreased whereas glucose variability was higher [85]. A similar study compared orange juice and cola consumption in between meals by healthy young adults. The orange juice consumption lowered day-long glycemia compared to the cola intervention. The two-week orange juice intervention did not affect body weight, fasting blood glucose, nor glucose tolerance [86].

To clarify the other points, high-fat high-carbohydrate (HFHC) meal challenges were conducted with healthy participants and concluded that orange juice ingestion along with HFHC decreases blood glucose responses compared to the isocaloric group and, despite the inherent high sugar content in orange juice, the change in blood glucose was similar to consuming water [87]. Another HFHC meal challenge in young healthy participants underpinned that orange juice intake modulated plasma miR-375 expression, which is a biomarker of pancreatic  $\beta$ -cell function and contributed to preventing hyperglycemia [88]. Another study compared meal challenges for a standard breakfast between lean and obese groups. Their results indicated that in the lean individuals, the blood glucose dropped by 11% for fresh orange juice and by 5% for processed orange juice, while for obese participants the blood glucose decreased by 13% after 60 min for both orange juices compared to the control drink [89]. For severely obese subjects, a 12-week orange juice daily consumption along with a reduced-energy diet improved insulin sensitivity, lipid profile, and their inflammatory status [90]. For a similar group, 12 weeks of orange juice intake as a snack accompanied by a balanced diet improved insulin resistance and mitigated their risk of metabolic syndrome by 30% [91]. Considering the impact of the orange juice composition, another study focused on fiber-enriched ones and highlighted that for healthy young subjects, Citrus fiber-enriched orange juice lowered postprandial glucose and postprandial insulin at 15 min compared to the one without fiber [92].

The latest meta-analysis of orange juice consumption concluded that the length of each study has an impact on the outcomes. Indeed, a study with an intervention longer than 8 weeks indicates an effect of *Citrus* consumption on T2DM biomarkers improvement. On the other hand, the increasing risk of T2DM related to orange juice consumption is due to the high intrinsic sugar content compared to raw fruit. Moreover, the juicing process lowers the end-product content in polyphenols and fibers. Additionally, the fluid nature of juices facilitates rapid absorption of sugars [93]. Though the short-term effects of orange juice in comparison with soda and/or with enriched fiber were shown to be beneficial in healthy subjects, the follow-up studies focusing on a longer-term impact highlighted a positive correlation with T2DM incidence in populations consuming orange juice on a regular basis. In this view, the authors believe that oranges are more beneficial when consumed fresh than as juice, especially for a diabetic population.

#### 3.3.3. Grape Juice

Grape juice is a popular and highly consumed beverage worldwide. A study on healthy overweight participants asked the participants to consume grape juice or a placebo juice for 8 weeks [94]. The results of this study showed that their blood glucose levels dropped after grape juice consumption and elevated after placebo juice consumption. In another study, postmenopausal participants were asked to consume white grape juice for 30 days. At the end of the study period, there was no change in blood glucose and blood insulin levels [95]. Concerning red grape juice, acute consumption by healthy subjects for a pilot study revealed no effect on blood glucose concentration. The same conclusions were highlighted when comparing acute consumption of red grape juice, organic grape juice, and water [96]. Though red grape juice is rich in polyphenols including resveratrol, quercetin, anthocyanin, proanthocyanin, and similar compounds, there are not enough clinical studies conducted in individuals with T2DM (Table 4). Thus, more studies need to be conducted before any recommendations can be made, especially since no information is available about grape juice GI and GL.

#### 3.3.4. Cherry Juice

A study in postmenopausal women with T2DM consuming concentrated sweet cherry juice daily for 6 weeks observed a decrease in HbA1c at the end of the study [97]. As cherries have a very low GI but cherry juice GI was not reported, individuals with T2DM can consume a moderate amount of cherries without any concerns.

#### 3.3.5. Pomegranate Juice

Pomegranate juice is an important derivative that enables safe long term of consumption of this highly anthocyanins-rich fruit. It was of interest to conduct a study using pomegranate juice and pomegranate juice concentrate (Table 4). In fact, a daily intake of pomegranate juice concentrate by T2DM patients for 3 months lowered their fasting blood glucose and increased Hb1Ac [98]. A more recent study with the same product consumed for 4 weeks concluded that it did not alter T2DM participants' glycemic parameters [99]. When consumed under the form of pomegranate juice for 6 weeks, T2DM participants had changes in fasting blood glucose, lipid profiles, lipoprotein oxidation, and PON1 (Serum paraoxonase and arylesterase 1) activity [100]. These results were confirmed by studies utilizing a longer intervention time, showing that 12 weeks in a similar population did not impair glycemic control nor HOMA-IR for diabetics and added to reduction in some inflammatory factors, namely IL-6 and hs-CRP [101,102]. Checking the effect of acute consumption of pomegranate juice by T2DM participants revealed a decrease in blood glucose level after 3 h of intake, and the intensity of hypoglycemic response depended on the participants' glucose starting level [103]. Further investigation of acute consumption showed that individuals with impaired glucose levels, but not individuals with normal glucose levels, experienced hypoglycemia. These T2DM participants also showed a decrease in melatonin, an increase in insulin, and an improvement of their insulin resistance [104]. A recent study investigated the effect of combined pomegranate juice consumption with a training program for T2DM participants. A noticeable improvement of insulin resistance and a decrease in liver enzymes was recorded for patients who consumed daily pomegranate juice and exercised three times per week [105]. Due to the adequate research, pomegranate juice is the healthiest juice among the fruits for diabetics. Based on the current research presenting an abundance of positive benefits on health parameters in a T2DM population, it is safe to promote pomegranate juice as the safest fruit juice to consume despite not having the exact GI and GL amount of the different variants of this juice. However, the authors suggest that, when possible, people should consume whole pomegranate rather than the juice.

| Fruit     | Study<br>Design   | Study Subjects  | Place | Duration                 | Fruit<br>Intervention                                    | Intervention Diet   | Significant Findings  | Reference |
|-----------|---|---|-------|--------------------------|--|---|---|-----------|
| Cherry    | quasi-<br>experimental<br>study                           | T2DM subjects<br>n = 20 F age:<br>$53.6 \pm 8.8$ y  | Iran  | 6 weeks                  | 40 g of<br>concentrated<br>sweet cherries<br>juice daily | Participants were<br>advised to keep their<br>usual diet and<br>physical activity<br>stable in the duration<br>of the trial.  | After six weeks'<br>consumption of<br>concentrated sweet<br>cherry juice, \_ in<br>HbA1c was seen.  | [97]      |
| Cranberry | Cross-<br>sectional                                       | Healthy subjects<br>n = 187 (38  M  149  F)<br>age: $19.7 \pm 0.13 \text{ y}$<br>BMI $23.8 \pm 1.03$<br>kg/m <sup>2</sup><br>no beverage/water<br>group $n = 46$<br>water group $n = 42$ ,<br>low-calorie Cranberry<br>juice<br>group $n = 43$<br>normal calorie<br>Cranberry juice<br>group $n = 40$ | USA   | Single-<br>dose<br>study | 1 serving = 480<br>mL/70 kg                              |   | Consumption of<br>low-calorie cranberry<br>juice is associated with<br>a favorable glycemic<br>response.  | [77]      |
| Cranberry | Double-blind,<br>randomized<br>control,<br>parallel trial | T2DM subjects<br>n = 58  M<br>Age: 54.8 $\pm$ 9.1 y, BMI<br>28.8 $\pm$ 3.6<br>kg/m <sup>2</sup>   | Iran  | 12 weeks                 | 240 mL of<br>Cranberry juice<br>or placebo drink         | Maintain usual diet<br>and physical activity<br>level and no<br>alteration to lifestyle.<br>Intake of 240 mL<br>daily for 12 weeks of<br>cranberry juice or<br>placebo drink. | Intake of cranberry juice<br>led to $\nearrow$ in apoA-I and<br>PON-1 activity and $\searrow$<br>in serum glucose and<br>apo B in T2D patients. | [79]      |

Table 4. A summary of clinical studies examining glycemic index and the intake of fruit juices.

| Fruit     | Study<br>Design  | Study Subjects  | Place  | Duration   | Fruit<br>Intervention  | Intervention Diet   | Significant Findings  | Referenc |
|-----------|--|---|--------|--|--|---|---|----------|
| Cranberry | Placebo-<br>controlled,<br>double-blind,<br>parallel arm       | Placebo group $n = 27$<br>(12 M 15 F)<br>age: 51.3 ± 11.1 y<br>BMI 29.1 ± 4.7 kg/m <sup>2</sup><br>Cranberry juice<br>group $n = 29$<br>(14 M 15 F)<br>age: 49.8 ± 11.3 y<br>BMI 27.8 kg/m <sup>2</sup> | USA    | 8 weeks  | 2 cups daily of<br>low-calorie<br>Cranberry juice<br>or placebo<br>beverage  | Intake of low<br>calorie-cranberry<br>juice or a<br>color / flavor / energy-<br>matched beverage 2<br>cups / d for 8 weeks.   | consuming the<br>low-calorie cranberry<br>juice ↘ fasting plasma<br>glucose, ↔ fasting<br>serum insulin.<br>Low-calorie cranberry<br>juice had a beneficial<br>effect on homeostasis of<br>insulin resistance for<br>participants with high<br>baseline values. | [78]     |
| Grape     | NS   | Subjects $n = 25$ F<br>age: 50–67 y BMI<br>indicating 44%<br>eutrophic and 40%<br>overweight  | Brazil | 30 days  | White grape<br>juice (7<br>mL/kg/day) in<br>2 to 3 portions  | Avoid consuming<br>grape derivate<br>products throughout<br>the intervention<br>period without other<br>changes in diet<br>energy consumption<br>or lifestyle.<br>Participants were<br>instructed to<br>consume 7<br>mL/kg/day of white<br>grape juice in 2 to 3<br>portions with<br>morning and<br>afternoon snacks and<br>dinner for 30 days.<br>Pilot: Refrain from  | Although white grape<br>juice has glucose and<br>fructose in its<br>composition,<br>supplementation with it<br>had no changes in BG<br>and BI.  | [95]     |
| Grape     | Pilot study<br>Randomized,<br>crossover<br>controlled<br>study | Subjects $n = 5$<br>(2 M 3 F) age: 20–55 y,<br>BMI 18–30 kg/m <sup>2</sup><br>Subjects $n = 24$<br>(19 F 5 M)<br>age: 20-55 y   | Brazil | Acute<br>consump-<br>tion<br>Three<br>acute<br>consump-<br>tions | 400 mL of red<br>grape juice<br>3 beverages:<br>conventional red<br>grape juice,<br>organic grape<br>juice and water | consuming<br>polyphenol-rich food<br>and beverages, such<br>as fruits, vegetables,<br>chocolate, tea, coffee,<br>honey, and alcoholic<br>beverages, for 3 days<br>before the experiment.<br>On the day of the<br>experiment, baseline<br>blood samples were<br>collected after 10-h<br>fasting. Subsequently,<br>volunteers were<br>given 400 mL of red<br>grape juice in a single<br>dose, and blood<br>samples were<br>collected periodically.<br>Crossover controlled:<br>In each intervention,<br>peripheral venous<br>blood samples were<br>collected after a 10-h<br>fasting as baseline<br>samples.<br>Subsequently,<br>participants were<br>given 400 mL of the<br>test beverage to<br>ingest within 5 min.<br>After 1 hour, another<br>blood sample was<br>collected. No food<br>was provided during<br>this period, and the<br>experiment was<br>repeated with the<br>other test beverages<br>after a washout<br>period of 14 days. | Despite the high<br>concentration of sugars,<br>the acute intake of<br>tropical grape juices did<br>not significantly affect<br>the concentrations of<br>glucose.   | [96]     |

| Fruit   | Study<br>Design            | Study Subjects   | Place  | Duration  | Fruit<br>Intervention   | Intervention Diet   | Significant Findings   | Reference |
|---|----------------------------|--|--------|---|---|---|--|-----------|
| Grape   | Double-blind,<br>crossover | Healthy overweight<br>subjects $n = 64$ Grape<br>first group $n = 30$<br>(19 M 11 F)<br>age: $41 \pm 13$ y BMI<br>28 $\pm 3.8$ kg/m <sup>2</sup><br>Placebo first group<br>n = 34 (25 M 9 F) age:<br>$44 \pm 11$ y BMI<br>28 $\pm 3.9$ kg/m <sup>2</sup> | USA    | 8 weeks   | Grape juice and<br>placebo beverage   | Participants were<br>asked to stop all<br>consumption of grape<br>juice, wine, grape<br>products, green or<br>black tea, dark juices<br>(e.g., cranberry and<br>pomegranate juice),<br>other<br>flavonoid-containing<br>beverages, and all<br>dietary supplements<br>for the duration of the<br>study. Participants<br>consumed each<br>beverage for 8 weeks<br>with a 4-week rest<br>period between<br>beverages.  | Glucose ∖, 2 mg/dL<br>after consumption of<br>grape juice and ≯<br>1 mg/dL after<br>consuming the placebo.   | [94]      |
| Orange/<br>apple/<br>grapefruit<br>juices<br>and<br>fresh<br>orange | Follow-up<br>studies       | Three prospective<br>longitudinal cohort<br>studies (Nurses'<br>Health Study<br>(1984–2008), Nurses'<br>Health Study II<br>(1991–2009), and the<br>Health Professionals<br>Follow-up Study<br>(1986–2008))   | USA    | Follow-<br>up<br>studies<br>for<br>different<br>durations | Orange/fruit<br>juices versus<br>fresh oranges<br>versus no juice<br>consumption  | 0   | Replacing fruit juice<br>with fresh oranges<br>the risk of T2D by 8%,<br>whereas one serving per<br>day of juice (apple,<br>orange, and grapefruit)  | [82]      |
| Orange  | Follow-up<br>study         | n = 7, 1346 F nurses<br>who were free of<br>cardiovascular<br>disease, cancer and<br>diabetes in 1984  | USA    | Follow-<br>up study<br>for 18<br>years                    | Orange juice<br>consumption   |   | Intake of fruit juices was<br>positively associated<br>with incidence of T2D.<br>Consuming more than<br>1 "cup" of orange juice<br><i>∧</i> the risk by 24%<br>compared to people<br>consuming less than a<br>"cup" of orange juice.               | [81]      |
| Orange  | Crossover                  | healthy participants<br>n = 12 (5 M 7 F) age:<br>25-45 y BMI 20-25<br>kg/m <sup>2</sup>  | Brazil | 3 meals<br>chal-<br>lenges                                | Each subject<br>consumed the<br>meal with either<br>500 mL of water,<br>100% orange<br>juice or an<br>isocaloric<br>beverage (water<br>with 57.5 g of<br>glucose) | All subjects received<br>a standard meal for<br>dinner the night<br>before the study and<br>fasted overnight ( $\geq 10$<br>h). In the morning,<br>consume a high-fat<br>high-carbohydrate<br>breakfast consisting<br>of a croissant with<br>butter and cheese<br>plus a chocolate<br>covered wafer (1037<br>kcal, 59% fat, 30%<br>carbohydrates, and<br>7% protein) with the<br>appropriate beverage.<br>Each test was<br>separated from its<br>precedent by at least<br>a one-week washout<br>period. | Orange juice ingestion<br>along with high-fat<br>high-carbohydrate S<br>BG responses compared<br>to the isocaloric group.<br>Despite the inherent<br>high sugar content in<br>orange juice, the change<br>in BG was similar to<br>consuming water. | [87]      |

| Fruit  | Study<br>Design                        | Study Subjects   | Place   | Duration   | Fruit<br>Intervention  | Intervention Diet   | Significant Findings   | Reference |
|--------|--|--|---------|--|--|---|--|-----------|
| Orange | Crossover,<br>free-living<br>nutrition | Healthy subjects<br>n = 26 (13  F 13  M)<br>age: 24.7 $\pm$ 3.2 y<br>BMI 23.2 $\pm$ 3.2<br>kg/m <sup>2</sup> | Germany | 2 weeks<br>and<br>minimum<br>1 week<br>wash- out<br>period | BM intervention:<br>3 times/day<br>in-between<br>meals<br>consumption of 1<br>cup of orange<br>juice WM<br>intervention:<br>consuming 1 cup<br>of orange juice<br>with meals | Subjects were<br>instructed to avoid<br>the consumption of<br>citrus fruits and any<br>additional orange<br>juice. A minimum of<br>1 week washout<br>period between the<br>2-week intervention<br>period.<br>Throughout<br>intervention periods,<br>participants were<br>asked to consume<br>only three meals a<br>day and drink orange<br>juice three times a<br>day either with meals<br>(WM) or in-between<br>meals (BM) for two<br>weeks. During the<br>BM intervention,<br>participants were<br>instructed to drink<br>the orange juice not<br>less than 2 h after<br>meals.<br>All subjects received<br>a standard meal a day | After between meals<br>intervention, fat mass<br>→ and PPI sensitivity<br>tended to ↘. By<br>contrast, after with<br>meals intervention fat<br>mass and<br>gamma-glutamyl<br>transferase ↘ whereas<br>glucose variability was<br>higher. | [85]      |
| Orange | Crossover                              | Healthy subjects<br>n = 12 (5  M 7 F)<br>age: 27.5 $\pm$ 7.5 y BMI<br>23.5 $\pm$ 2.0 kg/m <sup>2</sup>       | Brazil  | Meal<br>challenge  | 500 mL water or<br>pasteurized<br>orange juice   | a statutatu inear a day<br>before the study.<br>After fasting $\geq 10$ h,<br>participants<br>consumed a high-fat<br>high-carbohydrate<br>meal consisting of a<br>croissant with butter<br>and cheese plus a<br>chocolate-covered<br>wafer (1037 kcal, 59%<br>fat, 30%<br>carbohydrates, and<br>7% protein) with<br>500 mL of water,<br>100% orange juice or<br>an isocaloric<br>beverage after at least<br>one week washout  | A single high-fat<br>high-carbohydrate meal<br>with orange juice<br>modulated plasma<br>miR-375 expression,<br>which is a biomarker of<br>pancreatic β-cell<br>function and<br>contributed to<br>preventing<br>hyperglycemia.            | [88]      |
| Orange | Randomized<br>control trial            | Obese patients<br>n = 78 (24  M 54 F)<br>$age: 36 \pm 1 \text{ y}, \text{BMI}$<br>$33 \pm 3 \text{ kg/m}^2$  | Brazil  | 12 weeks   | orange juice<br>consumption<br>(500 mL/day)<br>and no orange<br>juice<br>consumption   | Individuals in the<br>orange juice group<br>were submitted to a<br>reduced calorie diet<br>that included orange<br>juice (500 mL/day),<br>and individuals in<br>the control group<br>were submitted to a<br>reduced diet without<br>orange juice for<br>12 weeks.   | Daily consumption of<br>100% orange juice<br>(500 mL/day) along<br>with a reduced-energy<br>diet for 12 weeks<br>significantly improved<br>insulin sensitivity, lipid<br>profile, and<br>inflammatory status in<br>obese subjects.       | [90]      |

| Fruit  | Study<br>Design  | Study Subjects  | Place  | Duration                       | Fruit<br>Intervention   | Intervention Diet   | Significant Findings   | Referenc |
|--------|--|---|--------|--------------------------------|---|---|--|----------|
| Orange | Semi-<br>randomized<br>control trial,<br>crossover                         | Lean group $n = 18$<br>age: 26.0 $\pm$ 7.6 y BMI<br>22.6 $\pm$ 1.8 kg/m <sup>2</sup><br>Obese group $n = 18$<br>age: 27.8 $\pm$ 7.6 y BMI<br>31.6 $\pm$ 5 kg/m <sup>2</sup> | Brazil | 3 meals<br>challenge           | Fresh orange<br>juice and<br>processed orange<br>juice 5 mL<br>juice /kg body<br>weight<br>Phase 1, fresh<br>orange juice;<br>Phase 2,<br>processed orange<br>juice;<br>Phase 3, energy<br>and sugar/acid-<br>matched,<br>orange-flavored;<br>Drink (Control) | Two days before the<br>trial, volunteers were<br>instructed to abstain<br>from alcohol, citrus<br>fruits, and juices,<br>maintain a moderate<br>level of carbohydrate<br>consumption and light<br>physical activity.<br>The subjects were<br>given 5 mL/kg body<br>weight of each<br>beverage in a 10-min<br>period, and after<br>30 min they had a<br>flavonoid-free<br>standard breakfast<br>containing: coffee<br>(infusion), skim milk,<br>sugar or sweetener,<br>white bread sandwich<br>with lean ham and<br>light cream cheese,<br>salted and sweet<br>biscuits.<br>Each phase was<br>separated from the<br>precedent by a 7- days | In lean individuals, the<br>BG was ∖ by 11% after<br>fresh orange juice and<br>by 5% after processed<br>orange juice. In obese<br>individuals, BG ∖ 13%<br>after 60 min of<br>processed and fresh<br>orange juice compared<br>to the control drink.  | [89]     |
| Orange | Randomized,<br>crossover,<br>double-blind,<br>placebo-<br>control<br>trial | healthy subjects<br>n = 10 (5  M 5 F) age:<br>$29.6 \pm 5.8 \text{ y}$<br>BMI 22.7 $\pm 0.5 \text{ kg/m}^2$   | Spain  | Two acute<br>consump-<br>tions | Fiber-enriched<br>orange juice and<br>orange juice<br>without fiber   | washout period.<br>Alcohol and beverages<br>containing caffeine<br>were ruled out and<br>subjects were<br>encouraged to<br>continue their usual<br>physical activities in<br>the days prior to the<br>interventions, but to<br>avoid intense activity.<br>The subjects were<br>recommended to<br>choose a standard<br>meal (1500–2500 Kcal)<br>and to consume it 24 h<br>before each<br>intervention.<br>After 12 h overnight<br>fasting, the<br>participants<br>underwent an acute<br>consumption test. The<br>second test was<br>conducted after<br>1–2 weeks.  | <i>Citrus</i> fiber-enriched<br>orange juice<br>significantly > PPG<br>and PPI at 15 min<br>compared to orange<br>juice with no fiber.<br>Despite a transient ><br>seen in glucose and<br>insulin responses in the<br>fiber group, no<br>significant differences<br>were seen in the peak<br>blood glucose (Cmax)<br>or AUC between the<br>two treatments.                                   | [92]     |
| Orange | Crossover,<br>quasi-<br>randomized-<br>control<br>trial                    | Healthy subjects<br>n = 26 (13  M  13  F)<br>age: 24.7 ± 3.2 y<br>BMI 19.1–33.9 kg/m <sup>2</sup>   | German | ny2 weeks                      | 100% orange<br>juice with pulp<br>and Caffeine-<br>free cola (1024<br>mL/day)   | During the<br>intervention periods,<br>consumption of<br>alcohol and additional<br>sugar-sweetened<br>beverages and fruit<br>juices was not allowed<br>and abstention from<br>consumption of citrus<br>fruits and citrus juices.<br>The subjects were<br>instructed to consume<br>the orange juice or the<br>cola between meals<br>(3 times/day) for<br>2 weeks separated by<br>one-two weeks<br>washout period.<br>After an overnight fast<br>( $\geq 10$ h), an oral<br>glucose tolerance test<br>was performed.  | Orange juice<br>consumption<br>significantly \scaleda daylong<br>glycaemia compared to<br>the cola intervention.<br>Orange juice<br>consumption for two<br>weeks did not<br>significantly affect body<br>weight nor FBG and<br>glucose tolerance in<br>healthy subjects<br>compared to a<br>caffeine-free cola<br>intervention (sugar<br>intake in both<br>interventions were<br>identical). | [86]     |

| Fruit  | Study<br>Design  | Study Subjects  | Place  | Duration                     | Fruit<br>Intervention   | Intervention Diet   | Significant Findings  | Reference |
|--------|--|---|--------|------------------------------|---|---|---|-----------|
| Orange | Controlled<br>non-<br>randomized<br>with<br>temporal<br>series<br>intergroup       | Healthy subjects<br>n = 10 F age:<br>$28.5 \pm 8.4$ y BMI<br>$24.1 \pm 3.3$ kg/m <sup>2</sup> | Brazil | 60 days<br>interven-<br>tion | Orange juice<br>consumption<br>300 mL/day                     | Three phases<br>(1) 30-day Basal<br>period: similar food<br>pattern for all<br>participants, without<br>restriction of energy,<br>avoiding rich sources<br>of flavonoids,<br>probiotics and<br>prebiotics, and<br>alcoholic beverages.<br>(2) Experimental<br>period of 60 days<br>consuming<br>300 mL/day of<br>orange juice.<br>(3) Washout of<br>30 days, without<br>orange juice.<br>All participants did<br>not consume fruits or<br>citrus juices or<br>alcohol for 3 days<br>before the start of<br>treatment with the   | Significant in BG,<br>triglycerides, total<br>cholesterol and LDL-C,<br>and HOMA-IR index<br>after 60 days, but<br>intermediate lower<br>values are observed at<br>the 30th day for all<br>variables, except LDL-C<br>that is significantly by<br>the 30th day. | [84]      |
| Orange | Parallel<br>group,<br>randomized<br>control trial                                  | Obese subjects $n = 72$<br>(23 M 49 F)<br>age: 48 $\pm$ 9 y<br>BMI > 30 kg/m <sup>2</sup>     | Brazil | 12 weeks                     | Orange juice<br>consumption<br>250 mL twice a<br>day as snack | orange juice.<br>The control group<br>was advised to<br>consume few citrus<br>fruits or citrus juices,<br>without exceeding<br>one serving per week.<br>The orange juice<br>group received 4 L of<br>juice weekly, and they<br>were instructed to<br>drink 250 mL as a<br>morning snack, and<br>250 mL as an<br>afternoon snack.<br>Three phases<br>(1) Orange juice-free   | Orange juice (100%)<br>consumption for<br>12 weeks along with a<br>"balanced diet"<br>improved insulin<br>resistance and mitigated<br>the risk of metabolic<br>syndrome by 30% in<br>susceptible subjects.  | [91]      |
| Orange | Controlled<br>clinical study<br>with<br>temporal<br>Series<br>intergroup<br>design | Healthy subjects<br>n = 10 F age:<br>$26.8 \pm 4.6$ y BMI<br>$24.1 \pm 3.3$ kg/m <sup>2</sup> | Brazil | 60 days                      | 100% orange<br>juice<br>(300 mL/day)                          | <ul> <li>(i) Orange juice-free</li> <li>diet: 30</li> <li>days with a habitual</li> <li>food pattern, without</li> <li>restriction of energy,</li> <li>avoiding rich sources</li> <li>of flavonoids,</li> <li>probiotics and</li> <li>prebiotics, and</li> <li>alcoholic beverages.</li> <li>(2) Diet plus orange</li> <li>juice: intervention of</li> <li>60 days consuming</li> <li>300 mL/day of</li> <li>orange juice.</li> <li>(3) Orange juice-free</li> <li>diet (Washout):</li> <li>30 days under a</li> <li>regular diet without</li> <li>orange juice.</li> </ul> | Significantly SFBG,<br>postprandial insulin,<br>and HOMA-IR after<br>60 days of daily<br>consumption of orange<br>juice.<br>After the washout, these<br>parameters returned to<br>their initial values.   | [83]      |

| Fruit       | Study<br>Design  | Study Subjects  | Place | Duration | Fruit<br>Intervention                           | Intervention Diet  | Significant Findings   | Reference |
|-------------|--|---|-------|----------|---|--|--|-----------|
| Orange      | Meta analysis  |   |       |          | Orange juice<br>consumption                     |  | The length of each<br>study appears to have a<br>major impact on the<br>outcome, with most of<br>the studies ≥8 weeks<br>indicating a possible<br>chronic effect of citrus<br>consumption in<br>improving biomarkers<br>of T2D risk.<br>The suggestion that<br>orange juice<br>consumption could <i>i</i><br>the risk of T2D is due to<br>the high intrinsic sugar<br>content and to the<br>relatively high glycemic<br>index compared to raw<br>fruit (glycemic load) per<br>serving.<br>The juicing process<br>results in reduced<br>(poly)phenol and<br>dietary fiber content,<br>and the fluid nature of<br>juices facilitates more<br>rapid absorption of<br>sugars, resulting in<br>pronounced glucose<br>and insulin responses.<br>These factors could<br>contribute to the<br>positive association<br>between citrus juice<br>intake and risk of T2D<br>observed in some<br>studies. | [93]      |
| Pomegranate | quasi-<br>experimental<br>interven-<br>tional<br>study | T2DM patients $n = 50$<br>The ratio of male to<br>female patients was<br>nearly the same age:<br>$45 \pm 8$ y BMI<br>$30 \pm 3$ kg/m <sup>2</sup> | Iran  | 6 weeks  | Pomegranate<br>juice<br>(200 mL/day)            | Blood was collected<br>from the patients<br>before and after<br>pomegranate<br>consumption after<br>12 h of fasting.   | Pomegranate juice<br>consumption may have<br>a contribution in<br>changing FBG, lipid<br>profiles, lipoprotein<br>oxidation, and PON1<br>activity.<br>FBG in the concentrate<br>pomegranate juice  | [100]     |
| Pomegranate | Quasi<br>experiment al<br>study                        | T2DM subjects $n = 55$<br>(11 M 22 F)<br>age: $50.6 \pm 9.3$ y<br>concentrate<br>pomegranate group<br>n = 33 control group<br>n = 22              | Iran  | 3 months | Concentrate<br>pomegranate<br>juice (40 g/day)  | The patients<br>consumed 40 g/day<br>of concentrate<br>pomegranate juice for<br>3 months. Control<br>group did not receive<br>experiment.  | group → compared<br>with the control group<br>but was not statistically<br>significant. HbA1c in<br>the concentrated<br>pomegranate juice<br>group → after the<br>intervention compared<br>with the control group<br>but did not statistically<br>significant.   | [98]      |
| Pomegranate | quasi-<br>experiment<br>trial                          | T2DM subjects $n = 31$<br>(15 M 16 F) age:<br>$46 \pm 8.3$ y BMI<br>29.53 $\pm$ 0.69 kg/m <sup>2</sup>  | Iran  | 4 weeks  | Concentrated<br>pomegranate<br>juice (50 g/day) | Patients were asked<br>to consume 50 g/day<br>of concentrated<br>pomegranate juice.<br>At the end of 4 weeks<br>intervention,<br>participants arrived<br>after overnight<br>fasting for<br>measurements. | In diabetic patients,<br>intake of concentrated<br>pomegranate juice does<br>not aggravate glycemic<br>parameters.   | [99]      |

| Fruit       | Study<br>Design   | Study Subjects  | Place  | Duration                  | Fruit<br>Intervention                           | Intervention Diet   | Significant Findings  | Reference |
|-------------|---|---|--------|---------------------------|---|---|---|-----------|
| Pomegranate | Randomized<br>control trial                                     | T2DM patients <i>n</i> = 85<br>(40 M 45 F)<br>age: 37–60 y Healthy<br>subjects <i>n</i> = 50<br>(25 M 25 F)<br>age: 30–60 y   | Jordan | Acute<br>consump-<br>tion | Pomegranate<br>juice 1.5 mL/kg<br>weight        | After 12 h fasting,<br>participants were<br>provided with fresh<br>pomegranate juice at<br>a dose of 1.5 mL/kg<br>to be consumed<br>within a 5-minute<br>time frame. Except<br>for water, subjects<br>were without food or<br>drinks for 3 h after<br>pomegranate juice<br>consumption. After 1<br>week, the same<br>procedure was<br>repeated on 23<br>randomly selected<br>subjects from the<br>patient group.<br>Alternatively, tap<br>water was consumed<br>at 1.5 mL/kg body | BG significantly ∖ in<br>T2D patients after 3 h of<br>pomegranate juice<br>consumption, compared<br>with the control.<br>This hypoglycemic<br>response depended on<br>initial FSG levels. The<br>effect of pomegranate<br>juice was also not<br>affected by the sex of<br>the patient and was less<br>potent in elderly<br>patients.      | [103]     |
| Pomegranate | Randomized,<br>double- blind                                    | T2DM subjects<br>n = 50<br>Pomegranate group<br>n = 22 (11 M 11 F) age:<br>$55 \pm 6.7$ y<br>BMI 29.4 $\pm$ 3.9<br>kg/m <sup>2</sup><br>Placebo group<br>n = 22 (12 M 10 F)<br>age: 56.9 $\pm$ 6.8 y<br>BMI 28.6 $\pm$ 4.2<br>kg/m <sup>2</sup> | Iran   | 12 weeks                  | Pomegranate<br>juice or placebo<br>(250 mL/day) | weight instead of<br>pomegranate juice.<br>Subjects were advised<br>not to change their<br>dietary habits,<br>physical activities, or<br>drug medication.<br>Participants in each<br>group<br>received either 250<br>mL/day<br>pomegranate juice or<br>a control beverage for<br>12 weeks.  | Pomegranate juice,<br>which is a<br>source of natural sugars,<br>does not affect FBG and<br>HOMA-IR in patients<br>with T2D, and it also<br>acts as an<br>anti-inflammatory<br>agent, lowering some<br>inflammatory factors<br>including IL-6 and CRP.  | [101]     |
| Pomegranate | Randomized,<br>double-blind,<br>placebo-<br>controlled<br>trial | T2DM subjects<br>n = 44<br>Pomegranate group<br>n = 22 (11 M 11 F) age:<br>$55 \pm 6.7$ y BMI<br>$29.4 \pm 3.9$ kg/m <sup>2</sup><br>Placebo group $n = 22$<br>(12 M 10 F) age:<br>$56.9 \pm 6.8$<br>y BMI 28.6 $\pm$ 4.2<br>kg/m <sup>2</sup>  | Iran   | 12 weeks                  | Pomegranate<br>juice or placebo<br>(250 mL/day) | The subjects were<br>asked not to change<br>their dietary habits,<br>physical activities, or<br>drug regimens. They<br>were assigned to their<br>respective groups<br>and asked to<br>consume 250 mL/day<br>either of<br>pomegranate juice or<br>placebo beverage for<br>12 weeks.  | Pomegranate juice<br>consumption<br>did not impair glycemic<br>control of diabetic<br>patients.   | [102]     |
| Pomegranate | Randomized<br>controlled<br>trial                               | Impaired fasting<br>glucose patients<br>n = 28 (10 M 18 F)<br>age: 29–56 y Healthy<br>subjects $n = 28$<br>(10 M 18 F)<br>age: 28–59 y  | Jordan | Acute<br>consump-<br>tion | Pomegranate<br>juice 1.5 mL/kg<br>weight        | Blood specimens<br>from each<br>participant were<br>collected before<br>5 min, and 1 and 3 h<br>after pomegranate<br>juice administration<br>at 1.5 mL/kg of the<br>body weight.  | People with impaired<br>fasting<br>glucose, but not healthy<br>individuals, had<br>significant<br>antihyperglycemic<br>response to<br>pomegranate juice 3 h<br>after ingesting the juice.<br>Fresh pomegranate<br>juice \_melatonin, /\_<br>insulin, and ameliorates<br>insulin resistance in<br>people with impaired<br>fasting glucose. | [104]     |

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|-----------|---|--|-------|----------|--|---|---|-----------|
| uit       | Study<br>Design   | Study Subjects   | Place | Duration | Fruit<br>Intervention  | Intervention Diet   | Significant Findings  | Reference |
| megranate | Single-blind,<br>placebo-<br>controlled,<br>randomized<br>trial | T2DM patients $n = 40$<br>age: 40–50 y AT + PJI<br>group $n = 10$<br>AT group $n = 10$ PJI<br>group $n = 10$ C<br>control group $n = 10$ | Iran  | 8 weeks  | Pomegranate<br>juice (PJI) (240<br>mL/day) after<br>lunch and/or<br>training program<br>(AT) | The AT program<br>consisted of 60–75%<br>of maximum heart<br>rate, 40–60 min/day<br>for 3 days/week.<br>Participants in the PJI<br>group consumed 240<br>mL of pomegranate<br>juice (sugar or<br>additive-free) daily<br>for 8 weeks.<br>Participants in the AT<br>and C groups | Due to the effect of<br>combined AT + PJI in<br>improving T2DM risk<br>factors, it could be<br>recommended for<br>T2DM patients to<br>prevent increased liver<br>enzymes and insulin<br>resistance. | [105]     |

Table 4. Cont.

received a water-based non-pomegranate placebo juice.

## 4. Conclusions

We conclude that when and where possible, diabetic individuals should consume fresh, and in some cases, dried fruit rather than juices, pulps, pomaces, and other fruit-derived products. It is also important for these individuals to take into account the quantity of fruit and fruit products consumed on any given day. It is easier to consume the calorically dense fruit products like juice in higher volumes than their fresh whole food forms, which leads to a higher daily total energy intake. We believe that the existing evidence on the supposed negative implication of juice consumption in metabolic disorders remains scarce, in addition to conflicting findings. This problem is due to the lack of randomized clinical trials that were appropriately adjusted for potential confounding variables, including total energy intake and physical activity levels, which are associated with the development of T2DM. To this end, this review will not only advance our understanding of the roles and effects of fruits and fruit-derived products on T2DM but will also illuminate and disentangle their relations to other cardiometabolic markers such as inflammatory responses, lipid profile, and antioxidative capacity and indices of glycemic control including insulin sensitivity, fasting blood glucose levels, and postprandial insulin levels.

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