

Postprandial metabolic events and fruit-derived phenolics: a review of the science

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There is increasing evidence that the postprandial state is an important contributing factor to chronic disease. The role of fruit phenolic compounds to protect health and lower disease risk through their actions in mitigating fed-state metabolic and oxidative stressors is of interest and the topic of the present paper. Two main questions are posed: first, what is the role of plant foods, specifically fruits rich in complex and simple phenolic compounds in postprandial metabolic management; and second, does the evidence support consuming these fruits with meals as a practical strategy to preserve health and lower risk for disease? This review provides an overview of the postprandial literature, specifically on the effect of fruits and their inherent phenolic compounds in human subjects on postprandial lipaemia, glycaemia/insulinaemia and associated events, such as oxidative stress and inflammation. Among the identified well-controlled human trials using a postprandial paradigm, >50% of the trials used wine or wine components and the remaining used various berries. Notwithstanding the need for more research, the collected data suggest that consuming phenolic-rich fruits increases the antioxidant capacity of the blood, and when they are consumed with high fat and carbohydrate 'pro-oxidant and pro-inflammatory' meals, they may counterbalance their negative effects. Given the content and availability of fat and carbohydrate in the Western diet, regular consumption of phenolic-rich foods, particularly in conjunction with meals, appears to be a prudent strategy to maintain oxidative balance and health.

Plant bioactives: Phenolics: Oxidative stress: Inflammation: LDL: Berries

During the past decade, it has become increasingly clear that oxidative stress and inflammation are key features in a number of chronic diseases, most notably those with metabolic roots. Plant foods, particularly fruits and vegetables, have been consistently identified in epidemiological research as the key components of dietary patterns that reduce risk for the development of chronic diseases, including atherosclerotic CVD, insulin resistance and type II diabetes and many cancers^(1–3). While total diet analyses take into account food–nutrient interactions and synergism between food components, it is of interest to examine specific food components that contribute to the total dietary effects. Bioactive compounds in foods that elicit physiologic responses to modulate processes of metabolism, oxidative stress and inflammation, which in turn promote health and reduce disease risk, are of particular importance and the focus of the present paper.

There is increasing evidence that the postprandial state is an important contributing factor to chronic disease^(4–9). The postprandial state is a dynamic period of metabolic trafficking, biosynthesis and oxidative metabolism of absorbed substrate, such as glucose, lipids, proteins and other dietary constituents. During this period, nearly every major biological system, organ, tissue and cell is responding with compensatory and

adaptive mechanisms managing the short-term disturbance to restore balance/homoeostasis. Under optimal conditions, the tilt from balance is modest allowing for rapid system recovery and negligible opportunity for unfavourable stress. In developed societies, there is ready access to nutrients and a modern lifestyle that favours excessive intake of energy, limited energy expenditure and de-emphasises the value of plant-based foods. This combined with the fact that most people eat several times a day results in exaggerated and prolonged metabolic, oxidative and immune imbalance, presenting opportunity for biological insult that over time could supersede biological defence and repair systems manifesting in cellular dysfunction, disease and ultimately death.

While the postprandial period presents opportunity for system disorder, particularly in light of modern eating patterns, this is also an opportunity for protection and intervention. Recently, we reported that consumption of flavonoid-rich strawberries delivered in a semi-liquid beverage along with a moderately high fat and carbohydrate meal, representing typical western eating patterns after an overnight fast, significantly reduced postprandial insulin and TAG responses and blocked the postprandial rise in oxidised LDL compared with consumption of a non-flavonoid-containing placebo beverage

Abbreviations: GSE, grape seed extract; NO, nitric oxide; ROS, reactive oxygen species.

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over a 6 h period in overweight men and women⁽¹⁰⁾. Of interest is that in the meal plus placebo beverage condition, the concentration of both oxidised LDL and inflammatory factors were still increasing at 6 h. By then (6 h) most people would have already eaten another meal. Hence, in the strawberry condition, the next meal would have been consumed against a background similar to the fasting (basal) state, whereas in the placebo condition, the next meal would have presented on a background where oxidised LDL and inflammatory factors were increasing, suggesting a probable compounding of an already activated postprandial state. Since western eating patterns include eating multiple meals a day, including snacks, one can only speculate on the level of biological unrest.

Given this background, two main questions arise. First, what is the role of plant foods, specifically fruits rich in complex and simple phenolic compounds in postprandial metabolic management; and second, does the evidence support consuming these fruits with meals as a practical strategy to preserve health and lower risk for disease? In an attempt to answer these questions, the postprandial literature has been reviewed to address the effect of fruits and their inherent phenolic compounds in human subjects on postprandial lipaemia, glycaemia/insulinaemia and associated events, such as oxidative stress and inflammation. It is anticipated that this discussion will extend our understanding of the diet/fruit–disease/health benefit relationship.

Fruit phenolic compounds: general background

The protective effect of fruit and vegetable intake has been attributed to the bioactivity of vitamins, minerals and fibre, and more recently, phytochemicals, particularly phenolic compounds^(11–14). Phenolic compounds are widely distributed throughout the plant kingdom and range from simple molecules such as phenolic acids to complex polymerised compounds (i.e. polyphenols)⁽¹⁵⁾. Flavonoids, together with phenolic acids, are a major subclass of polyphenols and are the most abundant polyphenols in the human diet^(15–19). The subclasses of flavonoids include flavonols such as quercetin and kaempferol, flavones (e.g. luteolin and catechins), flavan-3-ols (e.g. catechins), isoflavones (e.g. genistein), the anthocyanidins (e.g. pelargonidin) and the proanthocyanidins, to a name a few⁽¹⁵⁾. Flavonoids, along with other phenolic compounds, are believed to modulate several biological processes related to disease risk in human subjects including oxidative stress, platelet function^(20,21), inflammation^(22,23) and cancer initiation and propagation^(24,25). As such, these compounds have been implicated in promoting health by attenuating disease-inducing processes and have recently captured the interest of many health professionals, researchers, government agencies and even the lay public.

Fruit phenolic compounds: qualifying fruits

Fruits, like other plant foods, are natural vehicles of phenolic compounds; however, they differ remarkably in content, composition and bioavailability^(26–28). As such, there has been tremendous effort to provide a common system for qualifying and ranking fruits and linking this system to expected biological activity in human subjects. However,

so far, there is no unifying scheme that relates varieties of fruit to specific health benefits, specifically due to the incomplete nature of the available data.

Fruits may be classified based on the quantity of dominant phenolic compounds present in them; for instance, quercetin in apples and anthocyanins in strawberries. Fruits may also be classified by their antioxidant capacity using methods such as the Folin–Ciocalteu assay (expressed as total phenols content) or the Oxygen Radical Absorbance Capacity assay. An alternative system is based on the quantity and quality of antioxidants derived from phenols present in fruit, which is expressed as an index (PAOXI)⁽²⁹⁾. Free and total phenol quality is measured by the ability of the fruit to inhibit the oxidation of LDL and VLDL induced by cupric ion. Using this indexing system, Vinson *et al.*⁽³⁰⁾ evaluated the phenols present in twenty commonly consumed fruits in the American diet. They reported that among the twenty fruits tested, berries are the best source of polyphenol antioxidants, and therefore have the greatest likelihood of delivering an effect *in vivo*, since concentrations of fruit phenolic compounds in plasma are generally very low (1 µM or less). They also reported that fruits had significantly higher PAOXI values compared with vegetables. Whether higher PAOXI values of fruits translates to greater protection from chronic diseases compared with vegetables is uncertain.

Fruit phenolic compounds: present intake

Intake of phenolic compounds can range several fold depending on individual dietary patterns. Estimates of intake also rely on methods of assessment. Various estimates suggest American's consume 20 mg of flavonoids a day⁽¹⁶⁾, based predominately on flavonol and flavone intake, and up to approximately 190 mg daily⁽³¹⁾, based on intake of flavan-3-ols, flavanones, flavonols, anthocyanidins, flavones and isoflavones. In a dataset of ninety-two students using 7 d food records, Cao *et al.* (2009)⁽³²⁾ reported mean flavonol (quercetin and kaempferol) intake of 28.55 mg/d. Primary food sources included tea^(16,31), onions⁽¹⁶⁾, apples^(16,32), broccoli⁽¹⁶⁾, citrus fruit juices⁽³¹⁾, wine⁽³¹⁾, potato⁽³²⁾, celery⁽³²⁾ and citrus fruits⁽¹⁶⁾. Flavonols and flavones from other identified fruits/fruit sources, namely blueberries and strawberries, have been reported low, <1%⁽¹⁶⁾. In a seven countries report by Hertog *et al.*⁽³³⁾, flavonoid intake ranged from 2.6 mg/d in West Finland to 68.2 mg/d in Ushibuka, Japan⁽³³⁾. Consistent with the US reports, quercetin contributes most of the flavonoid intake, contributing >50% in most countries and up to 100% in West Finland⁽³³⁾. In our own estimates of dietary flavonoids intake using the United States Department of Agriculture Flavonoid database 2.1⁽³⁴⁾ and using dietary food intake records from a recently completed study in our lab (unpublished results), we found that the diets of pre- and post-menopausal women in the greater Chicago, IL, area contained anywhere from <1 mg/d to approximately 400 mg/d; or 0–292 mg/4184 kJ. Flavan-3-ol from tea intake contributed greatly to the higher dietary flavonoid intakes. Dietary flavonoids intake from meal plans taken from the dietary approaches to stop hypertension diet studies⁽¹²⁾ were estimated at approximately 4.6 mg/4184 kJ for the control diet and approximately 13.7 mg/1000 kcal for the dietary approaches to stop hypertension diet.

These estimates were calculated using the 2003 version of the United States Department of Agriculture Flavonoids database (version 2.0), of which only approximately 60 % of foods were found in the database. Additionally, the dietary approaches to stop hypertension diet was designed to target the action of non-flavonoid dietary constituents (K, Ca and Mg), but emphasised fruit and vegetable intake. Hence, dietary flavonoids intake, including classes of flavonoids, can vary immensely depending on food choice. An important additional consideration is timing of intake of dietary flavonoid and non-flavonoid phenolic compounds. Minimising the consequences of energy-dense meals may be an important feature of dietary phenolic antioxidant compounds on human health.

Fruit phenolic compounds: Mechanisms of action for health benefit

Fruit phenolic compounds may provide benefit to human subjects via several mechanisms⁽³⁵⁾. The best-described and most well-known mechanism is through their antioxidant properties and modulation of biological oxidative stress to prevent damage to cellular lipids, proteins and DNA. Directly, they may scavenge superoxide and other reactive oxygen species (ROS) such as hydroxyl and peroxy radicals. For example, from a thermodynamic standpoint, the chemical nature of flavonols lends them favourable to effectively scavenge superoxide anions, singlet oxygen and lipid peroxy radicals⁽³⁶⁾. Indirectly, some flavonoids may spare/recycle endogenous antioxidant (e.g. glutathione, urate, vitamin E and vitamin C) and selected flavonoids, such as catechins and quercetin, may chelate redox active metals, such as Fe and Cu, thereby removing a causal factor in free radical generation^(36–38). Flavonoid–metal complexes have also been reported to mimic superoxide dismutase activity providing another mechanism of ‘antioxidant defence’ benefit⁽³⁹⁾. However, the biological relevance of these described health-promoting mechanisms of flavonoid, such as free radical scavenging and metal chelation is questioned due to a kinetically unfavourable situation with respect to endogenous compounds such as glutathione, urate, vitamin C and a panoply of endogenous metal chelators that exist in plasma and tissues at much higher concentrations than flavonoid compounds (μM – mM v. nM –lower μM , respectively)⁽³⁶⁾. Similarly, questions have been raised about fruit-derived phenolics on the sparing or recycling of certain endogenous antioxidant defence compounds. Fruits deliver fructose along with phenolic compounds and some of the actions often ascribed to phenolics may be due to fructose. Fructose has been known for years to increase plasma urate levels through fructokinase-mediated metabolism to fructose 1-phosphate^(40,41). An increase in urate concentrations commensurate with increased plasma antioxidant capacity, which has been reported after strawberry, spinach and apple consumption^(42,43). Further, Lottito & Frei⁽⁴³⁾ reported parallel increases in urate and plasma antioxidant capacity after human volunteers consumed red delicious apples or fructose solution, each providing approximately 64 g fructose. Future studies on the antioxidant effects of flavonoid-rich foods should consider the effects of other non-phenolic contributors, such as the content of fructose, sucrose and sorbitol.

Indirect mechanisms of flavonoids involving lipid–flavonoid or protein–flavonoid interactions may be considered from a different perspective. Interactions requiring higher molecular specificity can withstand lower availability of substrate. Hence, alterations in membrane and protein function that involve lipid–flavonoid or protein–flavonoid interaction can happen at very low flavonoid concentrations and have significant biological effects at flavonoid concentrations attainable through diet. Stimulating endogenous antioxidant defence systems (e.g. superoxide dismutase and glutathione peroxidase) and/or inhibiting enzymes that generate large amounts of ROS such as xanthine oxidase and NAD(P)H oxidase are examples of ‘indirect’ antioxidant effects derived from protein–flavonoid interactions. Inhibiting absorption of already oxidised products, such as lipid hydroperoxides^(8,44), may be yet another mechanism of benefit by some phenolic compounds.

Over the last several years, polyphenolic compounds have been studied for their action in cellular signalling: modifying pathways of inflammation, insulin action, platelet function and vascular relaxation⁽³⁵⁾. For example, it is known that oxidants increase pro-inflammatory transcription factor NF- κ B, whereas antioxidants such as pyrrolidine dithiocarbamate and *N*-acetyl cysteine inhibit NF- κ B activation⁽⁴⁵⁾. Polyphenolic compounds from red wine have been shown to modulate NF- κ B activation, suggesting a redox-mediated action of red wine polyphenols on inflammatory pathways⁽⁴⁶⁾. Extracts of strawberry rich in anthocyanins have been shown to attenuate oxidative stress (H_2O_2)-induced impairment of insulin signalling by restoring insulin receptor substrate-1 activation in human skeletal muscle cells⁽⁴⁷⁾, an effect also shown in hepatoma cells with tea-derived (–)-epigallocatechin-3-gallate⁽⁴⁸⁾. Nitric oxide (NO)-stimulated endothelium-dependent relaxation by red wine, grape seed extract (GSE) and strawberries is due to activation of the protein kinase B (Akt)/phosphatidylinositol-3 kinase pathway, also well known for its regulation by cellular redox status^(49–51). Overall, phenolic compounds found in plant foods, including fruits, have multiple paths for benefiting human health, most notably, through their actions as antioxidants and modifying cellular events. Their specific actions are likely to be dependent on the composition and time course of compound-/metabolites appearing in plasma^(26,52,53). Continued advancement in technology and investment in research will help to elucidate these details.

The postprandial (fed) state

The postprandial state is a pro-oxidant state. The postprandial period is a time of active oxidative metabolism and formation of ROS. An imbalance between oxidant generation and antioxidant defence in favour of oxidants potentially leading to biological dysfunction and/or damage is referred to as oxidative stress. Postprandial hyperlipidaemia and hyperglycaemia induced by meals rich in lipids and carbohydrate induces a relative oxidative stress that is exaggerated and prolonged in individuals who are obese or diabetic^(5,7,54,55), highlighting the importance of insulin sensitivity. Postprandial oxidative stress is typically accompanied by postprandial inflammation and impaired endothelial function⁽⁵⁶⁾. Postprandial hyperlipidaemia and hyperglycaemia are risk factors for

cardio-metabolic disease, which is strongly associated with oxidative imbalance^(4,57–59). Therefore, consuming fruits rich in phenolic compounds with meals may have several advantages in the postprandial state, first and foremost, through their inherent antioxidant properties and potential to modulate cellular reductive–oxidative (redox) balance.

Several studies have shown that the phenolic compounds in fruit are bioavailable and can increase the antioxidant capacity of the plasma acutely and after long-term consumption^(26,60,61). However, this is not apparent in all studies^(62–66) and might be explained in part by the methods used to assess antioxidant capacity, experimental approach, dose, type of fruit and matrix, among other complex factors. Nonetheless, critical to the conclusion is the need to demonstrate changes in biological endpoints that indicate health and/or are involved in the pathology of disease. In light of the importance of postprandial glucose and lipid metabolism in health and disease risk, the effects of fruit on these parameters have been collated.

Postprandial glycaemia and insulinaemia

Postprandial hyperglycaemia is widely recognised as producing oxidative stress and is associated with exacerbating a number of disease and disease-related conditions, such as diabetes and atherosclerotic CVD, metabolic syndrome, hypertension and obesity^(57–59) as depicted in Fig. 1. Hyperglycaemia is associated with the generation of ROS and reactive nitrogen species, respectively, arising from several intracellular sources. In normal physiology, antioxidant

defence systems balance ROS/reactive nitrogen species. When these systems are overwhelmed, excess ROS/reactive nitrogen species alters redox balance increasing the activation of pro-inflammatory pathways (e.g. NF- κ B), impairing cellular signalling (e.g. insulin signalling) and causing irreversible modifications of cellular and non-cellular components⁽⁶⁷⁾. Hyperglycaemia can promote non-enzymatic glycation of proteins (Fig. 1), such as LDL⁽⁶⁸⁾, and can increase the susceptibility of LDL to oxidation^(69,70). Oxidised LDL is implicated in the initiation, progression and complication of atherosclerotic CVD^(71,72). Hence, strategies to modify postprandial glycaemia to favour a balanced system are warranted.

The glycaemic response to a meal is driven by preabsorptive and postabsorptive factors, including characteristics of the meal (dose and digestibility of carbohydrate, co-existing dietary factors and food matrix), alimentary metabolism and a variety of associated neuroendocrine responses, most notably the secretion and action of insulin to facilitate glucose clearance from the blood. The ability of fruits, based on their inherent phenolic composition, to favourably augment glucose metabolism would likely be through one of these factors. Interference with glucose absorption and/or modifying insulin-mediated glucose metabolism are two probable mechanisms; the latter having relevance in both glucose and lipid metabolisms and linking the antioxidant properties of fruit phenolics with cellular redox-sensitive pathways.

Few studies have examined the relationship between fruit phenolic compounds and postprandial glycaemia. Ten human

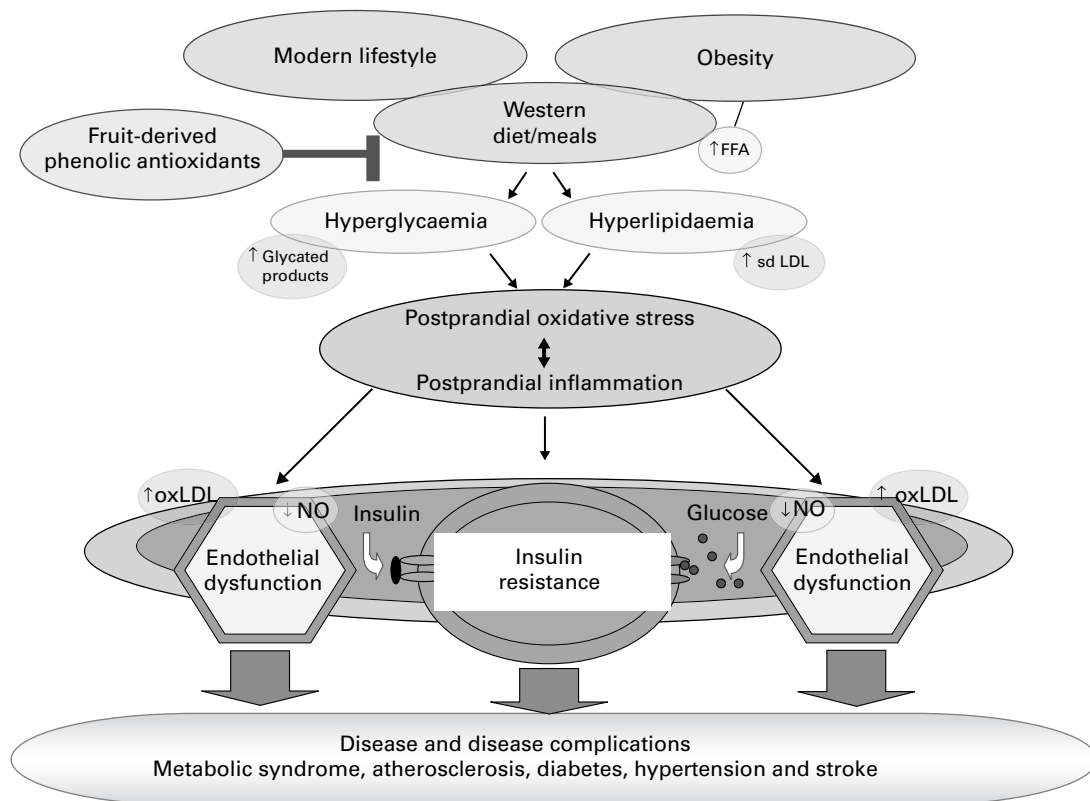


Fig. 1. Postprandial dysmetabolic-induced oxidative stress and possible mechanisms for fruit phenolic action. FFA, free fatty acid; sd LDL, small dense LDL; ox LDL, oxidised LDL; NO, nitric oxide.

Table 1. Clinical trials examining postprandial glucose and insulin responses after fruit-associated polyphenolic treatments

References	Study design	n	Subjects*	Fruit	Delivery†	Treatments	Dose	Glucose findings	Insulin findings	P
Ceriello <i>et al.</i> ⁽⁵⁴⁾	Within subject crossover 3 t × t 0–3 h	20	T2DM M, F	RW	Beverage + meal	Meal alone RW alone RW + meal Meal: 30 % fat 2510.4 kJ	300 ml total phenols, not specified	Gluc–	Ins–	NS, NS
Natella <i>et al.</i> ⁽⁷⁷⁾	Within subject crossover 2 t × t 0–3 h	6	Healthy M	RW	Beverage + meal	RW EtOH Meal: 24 % fat 40 % RMR × 1.5	400 ml 3.2 g/l total phenols	Gluc–		NS, NS
Naissides <i>et al.</i> ⁽⁷⁸⁾	Within subject crossover 3 t × t 0–6 h	17	Post-M dyslip OW F	RW	Beverage + meal	RW RW-de-alco water Meal: 53 % fat 1882.8 kJ	400 ml 2.2 g/l total phenols	Gluc–	Ins ↑	Gluc, NS Ins, P<0.05, RW v. water
Pal <i>et al.</i> ⁽⁷⁹⁾	Within subject crossover 3 t × t 0–6 h	8	Post-M dyslip OW F	RW	Beverage + meal	RW RW-de-alco water Meal: not specified‡	400 ml 2.2 g/l total phenols	Gluc–	Ins–	NS, NS
Kay & Colub ⁽⁷⁵⁾	Within-subject crossover 2 t × t 0–4 h	8	Healthy M	WBB	Beverage + meal	WBB Phenol-free Pbo Meal: 49 % fat 3568.952 kJ	100 g FD powder 14.7 mmol TE	Gluc ↑		P<0.05 WBB v. Pbo at 3 and 4 h
Cao <i>et al.</i> ⁽⁴²⁾	Within subject crossover 5 t × t 0–4 h§, 11 h	8	Healthy elderly F	RW	Beverage formula	RW Str spinach Vit C ctrl bev Beverage: 36 % fat 1046 kJ	300 ml 3.7 mmol TE	Gluc–		NS
Cao <i>et al.</i> ⁽⁴²⁾	Within subject crossover 5 t × t 0–4 h§, 11 h	8	Healthy elderly F	Str	Beverage formula	RW Str Spinach Vit C ctrl bev Beverage: 36 % fat 1046 kJ	240 g 3.7 mmol TE	Gluc–		NS
Vinson <i>et al.</i> ⁽⁷⁴⁾	Within subject crossover 2 t × t 0–4 h§, 7 h	10	OW M, F	CB	J + Vit C (80 mg)	CBJ + Vit C J Pbo + Vit C Beverage: 627.6 kJ	240 ml 175 mg total phenols	Gluc–		NS
Wilson <i>et al.</i> ⁽⁷³⁾	Parallel 6 t × t 0–3 h	187	Healthy M, F	CB	J LoJ (158.992 kJ) NmJ (1171.52 kJ)	Lo CB J Nm CB J LoHFCS J NmHFCS J water nothing Beverage: 158.992 or 1171.52 kJ	480 ml/70 kg total phenols, not specified	AUC Gluc–	AUC Ins–	NS, NS
Erdmann <i>et al.</i> ⁽⁷⁶⁾	Within subject crossover 5 t × t 0–4 h§, 5 h	14	Healthy M, F	Apple, kiwi, banana	Fresh fruit	Fat meal protein meal carb meal fruit meal veg meal	Mean (693 g)	Gluc–	Ins–	NS, NS

Fruit phenolics and postprandial metabolism

T2DM, Type 2 diabetes mellitus; RW, red wine; EtOH, ethyl alcohol; OW, overweight or obese; M, male; F, female; post-M, postmenopausal; dyslip, dyslipidaemia; Pbo, placebo; Glu, glucose; Ins, insulin; J, juice; Vit C, vitamin C; Str, strawberry; Ctrl bev, control beverage; WBB, wild blueberry; CB, cranberry; AUC, area under the curve; FD, freeze-dried; carb, carbohydrate; veg, vegetable; LoJ, low kcal juice; NmJ, normal juice; LoHFCS J, low high fructose corn syrup juice; NmHFCS J, normal high fructose corn syrup juice; ↓, decrease or reduction (P<0.05); ↑, increase (P<0.05); –, neutral; no effect (P>0.05) compared with placebo or baseline (i.e. comparator trials).

* Describes general health, age or weight status. Healthy indicates normolipidaemic, between 20 and 70 years, not overweight or obese and no documented disease or condition.

† Where meal is indicated, fruit or fruit-based beverage was consumed with the meal.

‡ Meal is likely the same as that provided in reference Naissides *et al.*⁽⁷⁸⁾.

§ Time point that a second meal was introduced. The results represent the glucose and insulin responses to this point.

trials were selected for the review (Table 1). These trials met criteria that included a minimum 2 h postprandial assessment of plasma glucose and included adequate controls or comparative data to evaluate the effect of the studied fruit on glycaemia. Criteria for delivery of fruit with a meal was desired, but was not mandatory given the small number of published trials. Cranberry juice^(73,74), wild blueberry⁽⁷⁵⁾, strawberry⁽⁴²⁾ and a fruit meal of banana, kiwi and apple⁽⁷⁶⁾ were the subject of five trials. Five additional trials were included that tested red wine or components of red wine with a meal^(54,77–79) or was a comparator in another study⁽⁴²⁾. Of these ten trials, six trials provided fruit as a beverage or in a beverage formula with meals^(54,42,75,77–79). As shown in Table 1, no remarkable effects on plasma glucose were reported overall. Only one trial reported a possible action in modifying glucose metabolism⁽⁷³⁾. In the trial by Wilson *et al.*⁽⁷³⁾, incremental area under the glucose curve after normal energy cranberry and energy control drinks was not different; however, the pattern of glycaemia was modified in the cranberry-containing drink, suggesting delayed absorption or altered distribution of glucose to insulin-sensitive tissues. Quercetin, a major phenolic compound in cranberry, has been shown to inhibit gastric uptake of glucose in a porcine model⁽⁸⁰⁾. Quercetin and myricetin have been demonstrated to inhibit GLUT-4-mediated uptake by adipocytes⁽⁸¹⁾; whereas insulin-sensitising actions of quercetin in liver and muscle have been reported in fructose-fed rat model of insulin resistance⁽⁸²⁾. Based on this limited evidence, no specific claims can be made relative to postprandial glucose control and cranberry or its associated phenolic compounds. Likewise, no evidence supports a glucose-lowering effect of consuming polyphenolic-rich fruits or beverages with meals. One trial reported an increase in postprandial glucose with wild blueberry consumption delivered in a beverage with a high-fat meal⁽⁷⁵⁾. The elevated glucose may be due to differences in mono- and di-saccharide content of treatments and/or the higher fibre content of the wild blueberry altering glucose absorption and metabolism. Insulin concentrations or other metabolic indices were not reported to help explain the results.

The postprandial insulin response is critical in the management of postprandial glucose metabolism as well as lipid and lipoprotein metabolisms. Insulin signalling is sensitive to cellular redox balance⁽⁸³⁾, suggesting that fruits rich in antioxidant compounds could beneficially impact nutrient metabolism through improved or enhanced insulin signalling in insulin-sensitive tissues. Five of the ten trials identified reported changes in postprandial insulin concentrations. Four reported no differences among treatments^(54,73,76,79) and one⁽⁷⁸⁾ reported elevated postprandial insulin concentrations after red wine consumption compared with dealcoholised red wine or water with a standardised meal of 75 g cheese and 50 g fat-free crackers in postmenopausal women. Recent work in our lab suggests that a strawberry-based drink delivering approximately 126 mg total flavonoids (approximately 82 mg anthocyanins) consumed with a moderate fat/carbohydrate meal reduces the postprandial insulin response in overweight men and women compared with when the same meal is consumed with a placebo (non-flavonoid containing) drink⁽⁸⁴⁾. No differences in postprandial glucose concentrations were observed between treatment conditions. These data suggest reduced insulin requirement to achieve glucose

homeostasis, supporting improved postprandial insulin sensitivity, an effect that appears to be mediated through redox-sensitive insulin signalling pathways^(82,84). More studies are needed to elucidate the potential effects of fruit phenolics on insulin action in human subjects.

Postprandial lipaemia

Elevated postprandial TAG are associated with increased risk for the development and progression of atherosclerotic CVD⁽⁸⁵⁾ and can be more discriminating than fasting concentrations in assessing high-risk atherosclerotic conditions⁽⁸⁶⁾. Fasting and postprandial hyperlipidaemia is apparent in individuals with obesity, diabetes mellitus and metabolic syndrome^(9,85,87). These conditions are also characterised by elevated NEFA, low-grade inflammation and impaired insulin sensitivity⁽⁴⁾, all of which promote and exacerbate disturbances in lipid metabolism. It is important to note that inflammatory mediators alone can trigger insulin resistance in cells, in the absence of obesity and other factors⁽⁸⁸⁾. For example, ingestion of a high-fat or glucose challenge meal provokes an acute inflammatory response^(83,89–92). Excessive intake of energy-dense, nutrient-poor foods provides potent substrate for inducing postprandial inflammation. Several lines of evidence, including work in our laboratory, suggest that the acute response arises from induction of oxidative stress and stimulated inflammatory pathways leading to reduced insulin sensitivity^(84,88–92) (Fig. 1). Under these conditions, lipaemia is magnified and the relative composition of all lipoproteins changes supporting an atherogenic state of the plasma. VLDL remnants are cholesterol ester enriched and in exchange, HDL become TAG rich and cholesterol depleted, which after further modification leads to the dissociation of the structurally important protein apo A-I, resulting in clearance and reduced HDL. Through a similar process, LDL become small and more susceptible to oxidation^(4,87). Oxidised LDL are proposed to play a causative role in early atherogenesis through their ability to up-regulate scavenger receptors on activated monocytes, transforming them into macrophages, eventually leading to foam cell formation⁽⁹³⁾.

Another aspect of postprandial lipaemia is endothelial dysfunction (Fig. 1). Many endothelial-derived factors, of which NO plays a central role, regulate vasomotion, permeability, proliferation and smooth muscle cell migration. Elevated TAG and NEFA are associated with reduced NO, a result that appears related to oxidative stress generation^(9,56). The oxidative imbalance results in reduced endothelial NO synthase activity and peroxynitrite generation and activation/up-regulation of NF- κ B and NF- κ B-dependent factors, such as monocyte chemoattractant protein-1, cellular adhesion molecules (e.g. intercellular adhesion molecule and vascular adhesion molecule), cytokines, growth factors and metalloproteinases, as well as pro-thrombotic factors including increased plasminogen activator inhibitor-1 and tissue factor to name a few⁽⁹⁴⁾. Overall, the lipaemia-induced oxidative stress promotes a pro-inflammatory, pro-thrombotic unstable atherogenic environment. In principle, preventing or decreasing the postprandial-induced oxidative stress or the associated inflammatory response should interrupt the metabolic–oxidative–inflammatory circle providing balance to the system and resistance to pathology. This may be one

mechanism by which eating fruits and vegetables regularly favour reduced disease risk.

Focused on fruits and their inherent phenolic quality to impart an action on postprandial lipaemia or associated events, fifteen trials using the postprandial testing paradigm were reviewed and are listed in Table 2. Changes in postprandial TAG were reported in twelve trials, of which one of the twelve trials⁽⁷⁹⁾ reported changes in plasma TAG and chylomicron (B-48) concentrations postmeal and another⁽⁴⁶⁾ reported changes in TAG, chylomicron and VLDL concentrations postmeal. Overall, seven trials reported no specific advantage on postprandial TAG management when consuming wild blueberry^(75,95), cultivated blueberry⁽⁹⁶⁾ or red wine^(54,77,79) or GSE⁽⁹⁸⁾ with a high/moderate fat meal (or whole milk⁽⁹⁶⁾). Serafini *et al.*⁽⁹⁶⁾ reported a 6% increase in total cholesterol at 5 h after consumption of 200 g blueberry with whole milk compared with the same dose of fruit with water; however, three other trials showed no changes in postprandial total cholesterol, LDL or HDL^(75,77,97). Three trials reported decreased postprandial TAG after consuming strawberry⁽¹⁰⁾, apple procyanidins (600 mg capsule)⁽⁹⁸⁾ and cranberry juice⁽⁷⁴⁾ with moderate fat, high fat or no fat meals, respectively. The TAG-lowering effect of fruits or their active constituents may have been by inhibition of pancreatic lipase activity⁽⁹⁸⁾, reduced dietary TAG absorption⁽⁷⁹⁾ and/or by enhanced clearance, possibly through antioxidant-mediated enhanced postprandial insulin sensitivity⁽⁹⁹⁾. Two trials reported elevated TAG when drinking red wine with a fat-enriched meal^(78,46). Increased postprandial TAG was evident after consuming red wine with alcohol compared with dealcoholised red wine or water⁽⁷⁸⁾ or after consuming a low-alcohol red wine or no wine⁽⁴⁶⁾, respectively, despite differences in trial population (postmenopausal dyslipidaemic women *v.* healthy young men and women). Elevation of VLDL indicates alcohol-induced stimulated hepatic lipogenesis with red wine⁽⁴⁶⁾; however, when alcohol (vodka) was controlled and the ratio of sugar to red wine alcohol varied (increased) at an equivalent energy level, VLDL was not increased compared with no wine with the fatty meal. These data suggest a threshold effect of alcohol plus sugar in stimulating hepatic lipogenesis or modifying clearance of VLDL. In either case, excess or prolonged circulation of TAG-rich lipoproteins, like VLDL, can be unfavourable, as discussed earlier. Interestingly, despite elevated TAG and VLDL after red wine consumption with a fat-enriched breakfast, Blanco-Colio *et al.*⁽⁴⁶⁾ reported reduced NF- κ B activation in cultured mononuclear cells in a time-dependent manner that was not evident in the no-wine or vodka conditions. Hence, components of red wine, presumably phenolic compounds, provided a relative protection from the potentially deleterious effects of the associated postprandial hyperlipidaemia.

Excessive metabolic substrate and dysregulated lipid (and carbohydrate) metabolism exposes cells to an overload of nutrients, generating a relative imbalance of ROS/reactive nitrogen species to antioxidant defences triggering a number of endogenous cellular responses that support and perpetuate the imbalanced state. The antioxidant properties of phenolic compounds in fruits and their contribution to the total antioxidant defence system are likely the underlying mechanism by which fruit consumption impart their greatest benefit. In the

case of lipid metabolism, the protection of LDL from oxidation is a critical matter. Elevated plasma concentrations of oxidised LDL are apparent in patients with CHD and diabetes and predict future risk of CHD events in apparently healthy men^(100–103). Several *in vitro* and *ex vivo* investigations (after feeding trials of days to weeks with fruit, fruit juice and wine) have demonstrated a relationship between increasing plasma antioxidant status and decreasing the susceptibility of LDL to oxidation^(104–109). In contrast, few investigations have examined acute protection of LDL, such as in a postprandial challenge paradigm. Postprandial LDL are more susceptible to oxidation than fasting LDL⁽¹¹⁰⁾ and postprandial LDL have been shown to accumulate more readily in activated macrophages than LDL derived from fasting samples^(71,110). The mechanism by which LDL become oxidised are not completely clear. Absorption of dietary-derived lipid hydroperoxides that incorporate into lipoproteins and act as initiators for further lipoprotein oxidative modification is one possibility⁽⁸⁾. The typical intake of lipid hydroperoxides in a fat-rich western diet has been estimated as 1.5 mmol/d⁽¹¹¹⁾. Consumption of polyphenols with a high-fat meal has been shown to decrease plasma lipid hydroperoxides. Natella *et al.*⁽⁹⁷⁾ showed in eight healthy men who consumed a standard 'Milanese' style meat and potatoes meal with (active) and without (placebo) 300 mg GSE that plasma lipid hydroperoxides were 1.5-fold higher in the placebo meal 1 h after the meal compared with the GSE active meal. Correspondingly, plasma antioxidant capacity was higher in the active GSE meal and resistance to LDL oxidation was enhanced, although statistical significance was not achieved between placebo and GSE active meals, a factor possibly due to timing of assessment and small sample size.

Circulating LDL is subject to oxidation in a pro-oxidative environment (postprandial state) when defences are inadequate. Acute protection may require direct association of antioxidant compounds with lipoproteins and/or activation of or preservation of the HDL-associated paraoxonase 1⁽¹¹²⁾. α -Tocopherol is a well-known lipid-soluble antioxidant present in LDL. Previous work has shown that dietary phenolic compounds can bind human LDL⁽¹¹³⁾. Phenolic compounds that bind LDL are likely to provide a relative protection of LDL from ROS through their peroxyl-scavenging activity or by structural modification resulting in *in vivo* resistance to oxidation^(114,115). Bound polyphenols may also spare losses of endogenous antioxidants, like α -tocopherol⁽⁷⁷⁾.

Present therapeutic strategies in CVD target improving serum cholesterol, generally LDL cholesterol, as assessed by fasting total and LDL concentrations. Because oxidised LDL is an early initiator and propagator of atherosclerosis, there may be merit in strategies that target protection of LDL from oxidation during the postabsorptive period. Trials with vitamin supplements such as vitamin E, vitamin C and β -carotene have been disappointing, possibly because they can act as pro-oxidants as well as antioxidants⁽¹¹²⁾. Long-term supplementation with polyphenolic compounds or polyphenolic-rich fruits on the susceptibility of fasting LDL has been disparate. Timing of intake (with or without a meal) may be one explanation for whether a favourable outcome will be achieved. Table 2 represents the few studies identified that measured oxidised LDL in plasma/serum after a meal that

Table 2. Clinical trials examining postprandial TAG and LDL oxidation responses after fruit-associated polyphenolic treatments

References	Study design	n	Subjects*	Fruit	Delivery†	Treatments	Dose	TAG findings	LDLox findings	Plasma AC with method	P
Ceriello <i>et al.</i> ⁽⁵⁴⁾	Within subject crossover 3 t × t 0–3 h-TAG 0–2 h-LDLox	20	T2DM M, F	RW	Beverage + meal	Meal alone RW alone RW + meal Meal: 30% fat 2510.4 kJ	300 ml total phenols, not specified	TAG–	LDLox–	AC ↑ ^TRAP	TAG, NS LDLox, NS AC ^P<0.001
Natella <i>et al.</i> ⁽⁷⁷⁾	Within subject crossover 2 t × t 0–3 h	6	Healthy M	RW	Beverage + meal	RW EtOH Meal: 24% fat kcal: 40% RMR × 1.5	400 ml 3.2 g/l total phenols	TAG–	LDLox ↓	AC ↑ ^TRAP	TAG, NS LDLox, P<0.05 AC ^P<0.003 Water v. RW P<0.02
Naissides <i>et al.</i> ⁽⁷⁸⁾	Within subject crossover 3 t × t 0–6 h	17	Post-M dyslip OW F	RW	Beverage + meal	RW RW-de-alco water Meal: 53% fat 1882.8 kJ	400 ml 2.2 g/l total phenols	TAG ↑			
Pal <i>et al.</i> ⁽⁷⁹⁾	Within subject crossover 3 t × t 0–6 h	8	Post-M dyslip OW F	RW	Beverage + meal	RW RW-de-alco water Meal: not specified‡	400 ml 2.2 g/l total phenols	TAG– CM ↓			TAG, NS CM, P<0.05 water v. RW-de-alco
Blanco-Colio <i>et al.</i> ⁽⁴⁶⁾	Within subject crossover 4 t × t 0–9 h	16	Healthy M, F	RW	Beverage + meal	RW, High dose RW, low dose Placebo Vodka Meal: 57% en fat 2518.768 kJ/m ²	M, 20 or 12 g/m ² F, 12 or 7.5 g/m ²	TAG ↑ CM ↑ VLDL ↑			TAG, P<0.05 CM, P<0.05 VLDL, P<0.05
Caccetta <i>et al.</i> ⁽⁶⁴⁾	Within subject crossover 4 t × t 0–4 h	12	Healthy and OW M	RW	Beverage + meal	RW RW-de-alco RW-phenol-strip water Meal: two plain bagels	5 ml/kg BW 2.0 g/l total phenols		LDLox–		NS
Burton-Freeman <i>et al.</i> ⁽¹⁰⁾	Within subject crossover 2 t × t 0–6 h	24	OW M, F	Str	Beverage + meal	Str Phenol-free Pbo Meal: 40% fat 2991.56 kJ	10 g FD powder 126 mg total phenols	TAG ↓	LDLox ↓		TAG, P<0.05 LDLox, P=0.008
Kay & Holub ⁽⁷⁵⁾	Within subject crossover 2 t × t 0–4 h	8	Healthy M	WBB	Beverage + meal	WBB Phenol-free Pbo Meal: 49% fat 3568.952 kJ	100 g FD powder 14.7 mmol TE	TAG–		AC ↑ ^ORAC ^^TAS/TEAC	TAG, NS AC at 1 h ^P=0.04 ^^P=0.05
Mazza <i>et al.</i> ⁽⁹⁵⁾	Within subject crossover 2 t × t 0–4 h	5	Healthy M	WBB	Beverage + meal	WBB phenol-free Pbo Meal: 49% fat 3568.952 kJ	100 g FD powder 14.7 mmol TE	TAG–		AC ↑ ^ORAC ^^TEAC	TAG, NS AC at 4 h ^P=0.04 ^^P=0.07 (1 h)
Natella <i>et al.</i> ⁽⁹⁷⁾	Within subject crossover 2 t × t 0–3 h	8	Healthy M	GSE	Capsule + meal	GSE, 300 mg Placebo Meal: 32% fat kcal: 40% RMR × 1.5	300 mg	TAG–	LDLox–	AC ↑ ^TRAP ^^Protein thiols ^^^Hydroperoxides ↓	TAG, NS LDLox, NS ^P<0.05 ^^P<0.05 ^^^P<0.05

B. Burton-Freeman

Table 2. Continued

References	Study design	n	Subjects*	Fruit	Delivery†	Treatments	Dose	TAG findings	LDLox findings	Plasma AC with method	P
Sugiyama <i>et al.</i> ⁽⁹⁸⁾	Within subject crossover 3 txt 0-6 h	6	Healthy M	AP	Capsule + meal	AP, 600 mg AP, 1500 mg Placebo Meal: 40 g fat 1673.6 kJ	600 mg 1500 mg 0 mg	TAG ↓			0 v. 600 mg <i>P</i> <0.05 at 6 h
Vinson <i>et al.</i> ⁽⁷⁴⁾	Within subject crossover 2 t × t 0-4§, 7 h	10	OW M, F	CB	J + Vit C (80 mg)	CBJ + Vit C J Pbo + Vit C Beverage: 627.6 kJ	240 ml 175 mg total phenols	TAG-		AC ↑ FRAP	TAG, NS AC <i>P</i> <0.05
Serafini <i>et al.</i> ⁽⁹⁶⁾	Within subject crossover 2 t × t 0-5 h	11	Healthy M, F	BB	Fresh fruit + whole milk	BB + milk BB + water Beverage: 543.92 kJ	200 g FW 250 mg total phenols	TAG-		AC ↑ ^TRAP ^^FRAP	TAG, NS AC at 5 h ^ <i>P</i> <0.05 ^^ <i>P</i> <0.001
Ziegler <i>et al.</i> ⁽¹¹⁶⁾	Parallel 4 t × t 0-24 h	60	Healthy	RW WW	Beverage	RW-1 RW-2 RW-3 WW	300 ml total phenols, not specified		LDLox-	Plasma Conjugated dienes- TBARS-	NS, NS

LDLox, LDL oxidation; AC, antioxidant capacity; M, male; F, female; RW, red wine; EtOH, ethyl alcohol; TRAP, total radical-trapping antioxidant parameter; post-M, postmenopausal; dyslip, dyslipidaemia; OW, overweight or obese; de-alco, de-alcoholised; CM, chylomicrons; Str, strawberry; Pbo, placebo; FD, freeze-dried; WBB, wild blueberry; ORAC, oxygen radical absorbance capacity; TAS, total antioxidant status; TEAC, trolox equivalent antioxidant capacity; GSE, grape seed extract; AP, apple polyphenol extract; CB, cranberry; vit C, vitamin C; BB, blueberry; J, juice; RW, red wine, WW, white wine; FRAP, ferric-reducing antioxidant power; TBAR, thiobarbituric acid reactive substances; ↓, decrease or reduction (*P*<0.05); ↑, increase (*P*<0.05); -, neutral, no effect (*P*>0.05) compared with placebo or baseline (i.e. comparator trials).

*Describes general health, age or weight status. Healthy indicates normolipidaemic, between >19 years, not overweight or obese and no documented disease or condition.

†Where meal is indicated, fruit or fruit-based beverage was consumed 5 d with the meal.

‡Meal is likely the same as that provided in reference Naissides *et al.*⁽⁷⁸⁾.

§ Time point that a second meal was introduced. The results represent the glucose and insulin responses to this point.

was accompanied by a phenolic-rich treatment or placebo. In relatively healthy individuals consuming a moderate-/high-fat meal, strawberry⁽¹⁰⁾ and red wine⁽⁷⁷⁾ blocked the postprandial rise in oxidised LDL or susceptibility of LDL to oxidation, respectively. GSE (300 mg capsule) with a high-fat meal in healthy men enhanced LDL protection, but this was not statistically different from the meal with placebo capsule⁽⁹⁷⁾. After a very low-fat meal (two plain bagels)⁽⁶⁴⁾ or no meal challenge⁽¹¹⁶⁾, changes in LDL oxidation were neutral, suggesting that the benefit of polyphenol consumption with a meal is to attenuate or block meal-induced oxidative stress when the stress is sufficient to result in oxidised LDL. In type 2 diabetic subjects⁽⁵⁴⁾, red wine attenuated meal-induced decrease in plasma antioxidant capacity (as measured by total radical-trapping antioxidant parameter) and partially protected LDL from the effect of the meal. Two investigations using a berry mix (240 mg; 80 mg each bilberries, lingonberries, black currant)⁽¹⁰¹⁾ or cactus fruit (500 g)⁽¹¹⁷⁾ compared postprandial LDL oxidation susceptibility with baseline (fasting) susceptibility measurements (no placebo or other comparator) after consuming fruit alone. Consumption of berries resulted in improved antioxidant capacity with neutral effect on LDL oxidative susceptibility. Cactus fruit, rich in peroxyl-scavenging betalains resulted in decreased susceptibility of LDL to oxidation at 3 and 5 h postprandially. The effect appeared dependent on betalain accumulation in LDL and sparing effects of lipid-soluble antioxidants. As with much of the postprandial effects of fruits and their inherent phytochemicals, additional research is required to understand betalains and indicaxanthins in health protection.

The acute effect of increasing antioxidant capacity of plasma is fairly consistent; however, changes in a biological marker of disease risk are not always indicated. This may be due to a variety of reasons ranging from composition and dose requirements to elicit an effect to choice of marker being measured. In addition, polyphenolic compounds likely act beyond a classic 'antioxidant' role to impart benefit, and hence changes in antioxidant capacity may not necessarily predict a biological response. Likewise, the interrelationship between acute and long-term effects of polyphenolic compounds on disease risk, as studied in various acute and chronic feeding paradigms, requires continued attention to better understand the translation and predictability of our models to describe biological impact and mechanism of action in a preventative or potentially therapeutic role in certain populations.

Other considerations

Obesity is a major risk factor for metabolic syndrome which is characterised by dyslipidaemia, dysglycaemia, hypertension, insulin resistance, obesity (particularly central adiposity) and elevated inflammatory markers⁽¹¹⁸⁾. Recent interest has focused on insulin resistance as a linking factor. Weight loss, as little as 5% of body weight, can dramatically improve metabolic endpoints, including insulin resistance. The recent discovery of ghrelin synthesis and secretion in human stomach has generated a new context to the regulation of food intake and potential treatment options for obesity⁽¹¹⁹⁾. Ghrelin is the only known peripheral signal that increases food intake. During fasting, ghrelin concentrations are elevated, and after

eating, ghrelin secretion is suppressed. Studies in human subjects indicate that ghrelin suppression is sensitive to meal composition and energy intake, rather than volume. Carbohydrate-rich meals appear superior to protein- or fat-rich meals in suppressing ghrelin concentrations postprandially⁽¹²⁰⁾. An inverse relationship between insulin and ghrelin suggests that foods or meals that elicit sufficient insulin will also suppress ghrelin⁽⁷⁶⁾. Fruit is a relatively carbohydrate-rich food; however, fruit is also low in energy, owing to its high water and indigestible carbohydrate content. Fruit delivers a variety of antioxidant compounds that could, via indirect redox-sensitive and anti-inflammatory mechanisms, influence postprandial insulin sensitivity. Improving postprandial insulin sensitivity would suggest a reduced insulin requirement with equitable glycaemic control, ghrelin suppression and managed appetite. Only one human trial was identified with exclusive fruit consumption in which ghrelin, insulin and glucose were measured in a postprandial testing paradigm⁽⁷⁶⁾. Because satiation (the process that brings eating to end) was a primary component of the study design, fruit intake was not fixed. Therefore, results are based on the mean intake of fruit consumed by participants (693 (SD 73) g, 434 (SD 188.3) kJ (45 kcal)). Compared with a bread-based carbohydrate meal (257 (SD 21) g, 658 (225.9) kJ (54 kcal)), the fruit (bananas, kiwi and apple) produced only a modest glucose and insulin response. Ghrelin was suppressed after fruit intake when insulin was elevated (45–60 min); however, unlike the bread meal, insulin concentrations rapidly returned to baseline concentrations and over the course of the next 3 h, ghrelin gradually rose eventually to above baseline concentrations during the last hour (3–4 h) before an *ad libitum* lunch was served. This trial generates several interesting hypotheses worth exploring further. It stands to reason that dietary strategies that improve antioxidant and inflammatory status for cardio-metabolic health would also prove advantageous for food intake and body weight regulation; however, randomised controlled trials are required to verify this relationship.

Conclusions

The role of fruit phenolic compounds to protect health and lower disease risk is a topic of great interest. There is a paucity of research to support a reliable understanding of fruit phenolics, among other sources of phenolic compounds, in postprandial metabolic events. It is clear that the postprandial state is a dynamic state of potential instability. Disturbances in postprandial metabolism of glucose, lipids and lipoproteins are linked to chronic disease. In a single day, the systemic stress of hyperglycaemia, hyperlipaemia and redox imbalance may seem trivial. Over time, however, these daily insults can lead to an array of complicated health consequences, atherosclerosis being at the top contributing to the more than 829 000 deaths a year in the United States⁽¹²¹⁾. Plant foods and particularly fruits rich in polyphenolic compounds may have a unique role in disease risk reduction through their actions in mitigating fed-state oxidative stressors that contribute to disease.

At the outset of this review, two main questions were posed: first, what is the role of plant foods, specifically fruits rich in complex and simple phenolic compounds in postprandial

metabolic management; and second, does the evidence support consuming these fruits with meals as a practical strategy to preserve health and lower risk for disease? With regard to both questions, an important finding of this review was the lack of human trials examining the effect of fruits rich in phenolic compounds on postprandial clinical endpoints. Advances in technology allow us to detect, quantify and pre-clinically screen compounds of relevance in fruit and human specimen. The present work is ongoing and being published. Additionally, however, well-controlled trials in defined populations considering subject characteristics, present health status and confounding factors related to complex food systems influencing polyphenol actions will be critical for making reliable conclusions to base dietary recommendations on fruit or fruit-based products for maintenance of health and disease management plans. Notwithstanding the need for more research, the collected data suggest that consuming phenolic-rich fruits increases the antioxidant capacity of the blood, and when they are consumed with high fat and readily available carbohydrate 'pro-oxidant and pro-inflammatory' meals, they may counterbalance their negative effects. Given the content and availability of fat and simple carbohydrates in the Western diet, regular consumption of phenolic-rich foods, particularly in conjunction with meals, appears to be a prudent strategy to maintain oxidative balance and health.

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