DISSERTATION

# PEELING BACK THE POTATO:

# AT THE INTERSECTION OF FOOD INSECURITY AND CARDIOMETABOLIC DISORDERS

Submitted by

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ABSTRACT

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According to the Centers for Disease Control (CDC), cardiometabolic diseases (CMD) such as cardiovascular disease and diabetes are the leading cause of death in the United States, which in turn, are strongly linked to obesity. Diet composition is known to be a primary contributing factor in the development of obesity, in the end promoting systemic chronic inflammation and CMD. Unfortunately, providing nutritious and affordable foods to Americans is still a challenge. This highlights the urgent need for additional research in both agriculture and nutrition, to provide sustainable, affordable, and high-quality foods which meet basic caloric and micronutrient needs. In recent years, much emphasis has been placed on phytochemicals due to their promising role in alleviating the pathophysiology of CMD. Phenolics have been proven to have direct health impacts such as increasing the antioxidant capacity of serum, reducing inflammatory biomarkers, ACE inhibitory, and improving arterial health.

Our research focused on the potato as it is a superior food choice for both health and nutrition per dollar. The explorations in this dissertation were conducted through multidisciplinary groups to evaluate the different aspects of potatoes, potential health benefits, and barriers to entry. Purple flesh genotypes showed the most antioxidant (AOX) activity, and the highest ACE inhibitory potential in-vitro. Importantly the observed variation within other market classes shall provide a great opportunity to improve these cultivars for the different sections of industry, beyond the fresh market. Beyond the bioactivity of the phytochemicals in-vitro, we examined the effect of

a whole potato (a high phenolics cultivar) diet on obesity and the subsequence pathophysiology. We observed that the high phenolic potato diet increased satiety in obese, leptin-deficient (ob/ob), mice. The obese mice on the purple potato diet also lost weight when compared to the obese with the control diet. The same trend was observed in the lean animal model (+/ob) who had the purple potato diet for 10 weeks. As a consequence of eating less, adiposity is reduced in both obese and lean animals. These observations were corroborated by a non-targeted metabolomics study of serum and liver in obese and lean animals, who had potato diet or control. Clear segregation was observed between the metabolites fingerprints between potato diet group compared to control diet. Reduction in serum cholesterol and liver triacylglycerol of the obese animal who had the potato diet was very promising.

In our last research, we sought the potato growers' decision-making process to adopt new cultivars or not. Each year, growers must decide in which cultivar to grow, and therefore this decision has an impact on the availability of a cultivar to consumers. This decision can be considered vital to public health as these cultivars are demonstrated to vary in traits important to human health. Adopting a new approach (either using new technology or adopting a new crop) brings risk to the system and is therefore associated with complex psychological and economic factors. We develop a multi-factorial model to explain adoption in a potato-growing system. Growers that were more aware of specialty cultivar innovation and associated consumer demand were more open to SCs adoption. Other influencing factors include a grower's experience selling a specialty cultivar in the previous year and access to diverse markets. Our model demonstrates that the current barriers to adoption are access to primary buyers such as warehouses, retailers, and households. Taken together, this research demonstrates how rational expectations stem from economic outcomes, knowledge, and experience in the potato industry. These results are important in helping to consider opportunities for growers to access new, higher-value markets, which may also improve consumer access to nutritious cultivars.

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# CHAPTER 1

## 1.1.Food security and public health

Sustainable physical, social, and economic access to sufficient, safe, and nutritious food, to meet population food preferences, and dietary needs for an active and healthy life is defined as food security (FAO, 2021). Through the 2030 sustainable development agenda, the world community is committed to 17 goals to end poverty and hunger, protect the planet, to foster peaceful, prosperous, and inclusive societies. Despite the effort to achieve these goals, countries are facing persistent challenges especially to end hunger and food insecurity. The moderate to severe food insecurity at the global level has been on the rise, from 22.6 percent in 2014 to 26.6 percent in 2019. The situation continued to worsen from 2019 to 2020, under the COVID-19 pandemic. In 2020, between 720 and 811 million people faced hunger, 161 million more than in 2019 (FAO; et al., 2021). This coupled with persistently high levels of income inequality put healthy diets out of reach for around 3 billion people (FAO; et al., 2021). In the US, 15% of the households were food insecure in 2020, ranging from 5.7 percent in New Hampshire to 15.3 percent in Mississippi (USDA/ERS, 2020). Colorado is among the states which food insecurity is near the US average (10.7%) (USDA/ERS, 2020). Several lines of evidence show the correlation between food insecurity and the growing number of multiple diseases. Food insecurity and malnutrition (low in micronutrients, high in refined grains, added sugars, saturated fats, and animal-source foods) increase the risk of obesity, insulin resistance, and eventually the development of metabolic disorders (FAO, 2019). Though the recent reports in the U.S. showing that access to nutritious, affordable, and desirable food to all consumers is still a big challenge (USDA, 2017). Food insecure households tend to consume high calorie, low nutrient diets and h`ave lower self-care behavior and poor metabolic control (Heerman et al., 2016, Berkowitz et al., 2013). Providing high-quality, nutritious food, especially for families with children, can prevent the population from a lifelong chronic disorder, and the countries from the incredible health care expenses. Finally, the COVID-19 pandemic and its interaction with obesity and other diet-related non-communicable diseases highlighted the urgency of ensuring access to affordable healthy diets for all.

### 1.2.Diet and cardiometabolic disease.

Besides providing calories, diet composition plays an important role in modulating disease risk, both acutely and in the long term. As such, an individual's dietary choices and habits can be used to predict disease risk. A Western-type diet, rich in animal protein, saturated fat, processed sugars, and refined grains, is associated with increases in circulating biomarkers of inflammation and metabolic dysfunction. Chronic consumption of a high-fat diet (HFD), traditionally low in plant-based foods, has been shown to promote metabolic dysfunction and inflammation through changes in intestinal permeability and shifts in the gut microbiome. Specifically, a HFD can increase intestinal permeability by inhibiting the expression of Tight Junction proteins (Turner-McGrievy et al., 2015, Cani et al., 2008). Additionally, high-fat foods stimulate addictive-like behaviors, such that these rewarding, yet unhealthy eating habits persist and even strengthen despite clear deleterious consequences (Sharma et al., 2013). In contrast to a HFD, strong and consistent evidence shows the beneficial effects of plant-based diets in alleviating metabolic risk factors (Kahleova et al., 2017, Dinu et al., 2017). A plant-based diet provides essential amino acids, proteins, carbohydrate and offer different proportions of fiber, essential micronutrients, vitamins, and minerals. Plant foods are also a rich source of bioactive compounds, i.e., phytochemicals, with the potential to promote health throughout the lifespan by reducing the risk of age and lifestyle-induced disease cardiometabolic diseases (CMD), such as cardiovascular disease (CVD) and type

2 diabetes (T2D), arise from a cluster of risk factors including hypertension, dyslipidemia, and insulin resistance (Leiter et al., 2011, Ross et al., 2020, Dagla et al., 2018). The development of which stems from obesity and associated metabolic dysfunction. CMD requires extensive medical treatment and long-term care and is considered the leading cause of death both in the US and globally (CDC and NCHS, 2021). Healthcare costs associated with the treatment of CMD total around $3.5 trillion annually in the US, making it a significant economic burden (CDC and NCHS, 2019). Obesity is considered a primary risk factor for CMD development, the prevalence for which continues to rise worldwide. Current estimates show that roughly 3 in 4 Americans are considered overweight or obese (CDC, 2018). A sedentary lifestyle, poor dietary patterns (e.g., 'Western-type' diet, high in saturated fat, sugar, and refined grains), and other environmental factors (e.g., socioeconomic status) have created an 'obesogenic environment' that continues to fuel the obesity pandemic. Diseases associated with obesity, like CMD, are driven largely by deleterious adaptations which occur broadly throughout the body, such as immune dysfunction, gut dysbiosis, dyslipidemia, and insulin resistance.

### 1.3.Potato: a sustainable solution to food insecurity

While various nutritional, pharmacological, and surgical interventions have been developed to mitigate the growing obesity pandemic and reduce CMD, more sustainable approaches to tackle this problem are needed. Improvements in public food security through greater access to affordable and nutritious foods are one possible solution. A broad definition for a sustainable and healthy diet is affordability, environmental sustainability, cultural acceptability, accessibility, and nutritional adequacy (FAO, 2012, Van Loo et al., 2017). This emphasizes the need to investigate and encourage health-promoting traits of the most affordable and highly consumed commodities, such as potatoes, to support a sustainable and healthy food supply for the broader population. As the number one consumed non-grain vegetable crop, the potato plays an important role in the US economy, with total fresh and processed potato production volume accounting for 3.7 billion dollars (USDA and NASS, 2017, USDA/ERS, 2019). The potato is an efficient crop and produces more dry matter, protein, and minerals per unit area than cereals (Ezekiel et al., 2013). As one of the most affordable vegetable options, that also meets the fundamental dietary guidelines for good health, the potato makes a great candidate for improving public food security and diet quality (CDCP, 2018).

Aspects of potato composition have been well studied. Specifically, they serve as an important source of vitamins and minerals, as 100 grams of baked potato (97 calories) contains 15% of the recommended amounts of vitamin B6, 16% of potassium, 9% of magnesium, and 6% of iron (Chaparro et al., 2018). Table 1.1. shows the chemical content in 100 grams of potato.

**Table 1.1.** potato nutritional value.

| | | **per 100 g cooked potato tuber fresh weight** |
|---|---|---|
| **Macronutrients** | Energy | 100 kcal |
| | Protein | 2 g |
| | Total lipids | 0.1 g |
| | Carbohydrates | 23 g |
| **Micronutrients** | Potassium | 411 mg |
| | Other Minerals | 147 mg |
| | Vitamin C | 15 mg |
| | B vitamins | 15 mg |
| | Free amino acids | 2.1 g |
| **Phytochemicals** | Phenolics (total) | 1 - 400 mg |
| | Phenolics (chlorogenic acids) | 1 - 100 mg |
| | Glycoalkaloids | 1 - 20 mg |

| | |
|---|---|
| Polyamines | 2 - 6 mg |
| Kukoamines | 3.5 mg |
| Calystegines | 0.3 – 6.8 mg |
| Carotenoids | 10 - 310 mg |
| Anthocyanins | 0.5 - 140 mg |
| Phytosterols | 5 mg |
| Nitrates | 1.5 - 50 mg |

**Table 1.1**. Adopted from Heuberger et al,. 2021. Values are often reported uncooked; some values are estimated based on 80% moisture conversion from reported dry weight values

Potatoes are also dense starch; however, their composition varies depending on the potato genotype. A portion of potato starch, specifically amylose, is resistant to digestion due to its chemical structure. Thus, these resistant starches reach the colon where they can be fermented by commensal bacteria and produce short-chain fatty acids (SCFAs) (Noda et al., 2008, Karlsson et al., 2007). In addition to their raw marketability, potatoes are also used frequently in the industry for making processed food products, starch, protein extract, and biofuel production (Hameed et al., 2018). More so, potato fiber and protein are valuable by-products from the food processing industry, which have been used as food additives with nutritional benefits (Ben Jeddou et al., 2017). The potato is clearly in an economic and societal position to provide extended benefits.

Now we shall dive into its bioactive chemicals and more specifically peptides in different genotypes, and how to cultivate such unique and advantageous properties for health benefit.

## 1.4.Variation in potato genotypes

In addition to conventional cultivars, specialty/value-added cultivars have been developed by breeding programs with demonstrated health benefits, supported by several clinical research initiatives. Studies on different potato genotypes have identified diverse phytochemical (phenolics, anthocyanins, alkaloids, etc.) and macronutrient (protein and carbohydrate) highlighting their uniqueness (Jansen and Flamme, 2006, Andre et al., 2007a, Stushnoff et al., 2008, Bártová and Barta, 2009, Bártová et al., 2015, Chaparro et al., 2018). For example, key minerals essential for human development are shown to vary greatly among market class, iron (up to 6-fold), zinc (4.5-fold), calcium (6.7-fold) (Andre et al., 2007a, Subramanian et al., 2017, Chaparro et al., 2018). Similar variation has been demonstrated in potato phytochemical content, such as phenolics, with some genotypes having up to 40-fold higher concentrations (Andre et al., 2007a, Zhu et al., 2010, Deußer et al., 2012, Chaparro et al., 2018).

However, the variation in the chemical composition of potato genotypes is not limited to just small molecules, as macronutrients like protein and carbohydrate (starch and resistant starch) content also vary among different genotypes (Dobson et al., 2008). Considering our understanding of the variation between different potato genotypes in phytochemicals, protein, and amino acids (AA), and carbohydrate content, it seems reasonable to suspect that their health outcomes also vary. In combination with growing public and medical interest to provide affordable foods that meet micronutrient and calorie requirements for better health, further research, and development in breeding programs for specialty/value-added cultivars is needed. However, our understanding regarding the effect of potato genotype variation in bioactives alone or in whole food matrices, on metabolic pathways and CMD risk factors is still limited. This ***knowledge gap*** greatly delays our clinical translation to the agricultural and food industry. Thus, it is imperative to expand our understanding of genotype-related variation in bioactivity and effect on health outcomes and enhance the supply chain for plant-based foods with an emphasis on potatoes.

## 1.5.The long-term goal of this research

The long-term goal of my research is to improve our understanding of potato as a functional food. The result of my work will impact various stakeholders including basic science researchers, dietitians, growers, consumers, and policy-makers. Importantly, my results will lay a foundation to drive future breeding efforts as well as pre-clinical research to optimize potato genetics for human health. To address this long-term goal my research sought:

1. Characterize the variation in phenolic content within potato genotypes spanning the five market classes and evaluate the impact of cooking on the bioactivity of phenolic compounds. I hypothesize that that genetic variation will correlate with variation in in phenolic content and that bioactivity will be reduced by cooking.
2. Characterize the impact of potato as a whole food on cardiometabolic health using a rodent model of obesity. I hypothesize that a high phenolic potato diet will influence metabolism and result in an improvement in health biomarkers compared to a control diet and that these effects will be variable between lean and obese animals.
3. Investigate the reasons that growers are slow in adopting the new varieties despite their demonstrated nutritional value. I hypothesize that socioeconomic, social, and cognitive factors influence the decision-making process for growers to adopt specialty genotypes in potatoes.

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# CHAPTER 2:

# INVESTIGATIONS INTO THE VARIATION IN THE BIOACTIVITY OF SMALL MOLECULES IN VARIOUS POTATO GENOTYPES. CASE STUDY OF ANTIOXIDANT AND ACE INHIBITORY ACTIVITY OF POTATO PHENOLIC COMPOUNDS

## 2.1. Introduction

Blood pressure is defined as the force exerted upon the blood vessels walls by blood ejected from the heart. Blood pressure is comprised of two components, systolic (the force exerted during each heartbeat) and diastolic (the force exerted in between heart beats). Hypertension is defined as systolic blood pressure (SBP) of 140 mm Hg or higher or diastolic blood pressure (DBP) of 90 mm Hg or higher (AHA, 2022, Dzau and Balatbat, 2019). Having hypertension increases the risk for heart disease and stroke, which are leading causes of death in the United States. In 2019, more than half a million deaths in the United States listed hypertension as a primary or contributing cause (CDC and NCHS, 2021). High blood pressure costs the United States about $131 billion each year, averaged over 12 years from 2003 to 2014 (CDC and NCHS, 2021). Hypertension, if not regulated, can lead to other cardiovascular problems such as heart failure, chronic kidney disease (Fuchs and Whelton, 2020).

Blood pressure is highly regulated via various complementary mechanisms. The kidney is generally considered to play the greatest role in blood pressure regulation The relationship between kidney function and hypertension was first discovered by Richard Bright in 1838. He observed that patients dying with contracted kidneys often exhibited a hard, full pulse, and cardiac hypertrophy (Marks and Maxwell, 1979). This discovery was neglected until the late nineteenth century when Tigerstedt and Bergman observed that aqueous extracts of kidneys caused a prolonged rise in the blood pressure of anesthetized animals. While they did not isolate a single compound from the extract responsible for this effect, they referred to the active compound as "renin" in reference to the kidney (Basso and Terragno, 2001). Today it is clear that the kidney regulates blood pressure by controlling body fluid volume. Sodium reabsorption and potassium excretion in the kidney leads to a rise in the osmolarity level and a subsequent increase in blood volume. Different parts of nephrons are controlled by the sympathetic nervous system (SNS) which senses the chemical composition of the blood and controls fluid reabsorption (Pontes et al., 2015).

The renin-angiotensin (Ang)–aldosterone system (RAAS) is a vital hormonal system housed within the kidneys that helps to regulate blood pressure. Specifically, the RAAS tightly regulates arterial pressure, vascular tonicity, and kidney function (Patel et al., 2017, Mirabito Colafella et al., 2019). Bioactive peptides synthesized by the RAAS have been demonstrated to impact hypertension and are involved in the development of other cardiovascular pathophysiology conditions in both animal and human studies (Hussain and Awan, 2018, Marc and Llorens-Cortes, 2011).

The RAAS cascade starts with renin biosynthesis in juxtaglomerular cells (JG) in the afferent arteriole, resulting in two forms of inactive prorenin and active renin. While the kidney is the only tissue known to produce active renin, inactive prorenin is produced in tissues tissues including the adrenal gland, ovary, testis, placenta, retina, and the brain (Atlas, 2007, Xu et al., 2016). Active renin is released to the plasma in response to a decrease in renal perfusion, sodium chloride concentration, and sympathetic nervous system activity (Atlas, 2007). Renin circulates and cleaves its only known substrate, angiotensinogen (Agt), which is primarily synthesized in the liver. Proteolytic cleavage of Agt results in the decapeptide angiotensin I (AngI), which is later metabolized to an octapeptide, angiotensin II (AngII), by the the enzyme angiotensin converting enzyme (ACE) (Mascolo et al., 2017, Unger, 2002).

### 2.1.2. Role of angiotensin II in controlling blood pressure

AngII is a multifunctional molecule with a prominent role in the central regulation of blood pressure through various avenues. For example, it is known to be a tonic stimulus of renal sympathetic nerve activity. Alongside the SNS, the kidney controls sodium and potassium balance through biosynthesis of aldosterone. Aldosterone, a hormone produced in the cortex of the adrenal gland, regulates sodium reabsorption and potassium excretion at the distal tubule and collecting duct of the nephron. Together, plasma sodium and potassium concentration and AngII control aldosterone release, leading to a long-term effect on blood pressure (Kaschina et al., 2018, Fountain and Lappin, 2020, Yatabe et al., 2011). Blood chemical composition, i.e. blood sodium, can evoke the production of renin in juxtaglomerular (JG) cells in the afferent arterioles which eventually increases the concentration of AngII in the circulation (Atlas, 2007). Elevated levels of AngII result in stimulation of receptors in the preglomerular and afferent arterioles and increase local vasoconstriction as well as sodium reabsorption (Gao et al., 2015, Pontes et al., 2015). AngII also mediates kidney vasoconstriction through cyclooxygenase (COX) related prostaglandin E (2) release in the kidney, which eventually contributes to augmented distal Na+ reabsorption and the development of hypertension (Gonzalez et al., 2014, Doller et al., 2009, Gonzalez et al., 2017). Another function of circulating AngII, is to increase blood-brain barrier permeability and induce stimulation of sympathetic nerve activity and induction of neurogenic hypertension (Biancardi et al., 2014, Guimarães et al., 2019, Ren et al., 2019).

Finally, AngII is also involved in calcium signaling, which in turn helps control vascular smooth muscle cell (VSMCs) function. The VSMCs, unlike cardiac or skeletal muscle cells, change their phenotype in response to environmental stimuli from a differentiated and contractile state to a synthetic state which lacks contractile properties (Liu et al., 2020, Lu et al., 2018). Increased activity of calcium channels in vascular smooth muscle cells leads to the promotion of actin-myosin bridge formation and VSMC contraction (Trebak et al., 2009, Zhang et al., 2012, Touyz et al., 2018). Chronic overactivation of calcium channels can participate in the development and progression of cardiovascular diseases, including atherosclerosis.

Various hormones, vasoactive peptides, and reactive oxygen and nitrogen species (RONS), affect VSMC and endothelial cell homeostasis (Touyz et al., 2018, Loke et al., 2008). For example, elevated AngII stimulates expression of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX), which in turn leads to synthesis of inflammatory mediators. Together these mediators induce vascular remodeling and susceptibility to hypertension (Mehta and Griendling, 2007, Dinh et al., 2017, Husain et al., 2015, Zimmerman et al., 2004, Griendling et al., 1994).

### 2.1.3. Oxidative stress and inflammation, the underlying cause of CMD

Oxidative stress can be described as a disruption in the steady state of free radical production and antioxidant defense (Betteridge, 2000, Halliwell, 2007). Under normal conditions, RONS are produced endogenously in all aerobic cells and act as signaling molecules in various physiological pathways. Exogenous sources also introduce molecules to the system which can be metabolized into free radicals in the body (e.g., air or water pollution, drug, industrial solvents, etc.) (Genestra, 2007, Liguori et al., 2018). The endogenous antioxidant system (AOX) maintains these reactive molecules at very low concentrations as they are needed for several signal transduction cascades (such as monitoring the intracellular level of stress or damage). Despite this, several pathological situations can result in sustained production of reactive molecules at levels that exceed the antioxidant capacity of the organism. The disruption in the RONS homeostasis results in oxidative stress which can inflict oxidative damage to cellular biomolecules, such as proteins, lipids, and nucleic acids DNA (Liguori et al., 2018, McCord, 2000, Valko et al., 2006). These altered molecules act as signaling components in the pathogenesis of CMD complications. For example, one of the early biomarkers of cardiovascular development is an accumulation of oxidized low-density lipoprotein (OxLDL) (Scioli et al., 2020), and oxidative-induced DNA lesions are one of the biomarkers of cancer development (Loft et al., 2012, Matter et al., 2018, Valko et al., 2006).

Increased levels of RONS play a major role in CMD complications mainly by induction of systemic chronic inflammation. Crosstalk among oxidative metabolism and inflammatory pathways has been established in several epidemiological studies (REF). Oxidative products signal and initiate the recruitment of pro-inflammatory RONS, cells, and cytokines at various stages of chronic inflammation, and at the same time induce further RONS production. RONS signaling can drive the activation of immune cells, such as the development of T cells and cytokine production, resulting in anti-inflammatory phenotype (Kesarwani et al., 2013, Abimannan et al., 2016). Other studies have shown that redox-sensitive transcription factors, such as NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) are activated by excessive production of RONS and subsequent inflammatory responses (Lingappan, 2018, Shanmugam et al., 2016, Fiers et al., 1999). NF-κB signaling pathways are an important upstream stimulus for the production of proinflammatory mediators such as TNF- α (tumor necrosis factor), interferon (IFN)-γ (Tang et al., 2019). These inflammatory cytokines further activate other pro-inflammatory genes and mediate inflammatory responses in various tissues. The activation of immune cells or proinflammatory signals circle back and induce further RONS production (e.g., leukocytes activation) (Vaziri and Rodríguez-Iturbe, 2006, Espín et al., 2017).

On the other hand, substances induced from chronic disorders such as diabetes, cancer, also induce oxidative stress in the system. For example, a chronic hyperglycemic state can lead to an increase in the levels of oxidative stress-induced DNA damage markers (Valavanidis et al., 2009, Dabrowska and Wiczkowski, 2017, Valko et al., 2006), lipid and protein oxidation products (Fraga et al., 1988, Ghorbanzadeh et al., 2016), and also lower the activity of antioxidant enzymes (Sakai et al., 2003, Mahalakshmi and Kurian, 2018). Accumulation of substances related to diabetes (e.g advanced glycation end products (AGEs) and their signal-transducing cascade) can evoke oxidative stress and subsequently elicit vascular inflammation (Yamagishi and Matsui, 2010, Yiu et al., 2016, Saroj et al., 2020). In obese individuals, excess adipose deposition is linked to increased free radical-mediated oxidative stress (Le Lay et al., 2014, Manna and Jain, 2015) and a decrease in endogenous AOX enzyme production and activity (Park et al., 2010). Reduction in AOX activity has been detected in other CMD, including hypertension and endothelial dysfunction (Steven et al., 2019, Brown et al., 2007). Taken together, these observations indicate the vicious cycle of oxidative stress, inflammation, and CMD.

### 2.1.4. Phenolic compounds: origin, and classification

It has been clearly demonstrated that dietary patterns influence health and that a diet high in plant food is associated with a lower risk of CMD (Kim et al., 2019). The positive health outcomes associated with a diet rich in fruits and vegetables are strongly correlated with the phytochemical content of these foods. As such, the Dietary Phytochemical Index (DPI) – defined as the percentage of calories supplied from phytochemicals in fruits, and vegetables - is associated with a reduction of CMD risk factors (McCarty, 2004, Farhangi et al., 2017, Kim and Park, 2020, Eslami et al., 2020).

But what are phytochemicals? The plant kingdom is the source of phytochemicals and other biologically active molecules, including peptides and small molecules (smaller than 10000 kilodaltons). In plants, phytochemicals are non-essential compounds (secondary metabolites) that that can impact multiple cellular metabolism and signaling pathways. Today, phytochemicals are at the center of drug discovery and dietary recommendations and the characterization of phytochemical sources, biological activity and pharmacognosy of phytochemicals is an active area of research.

More than 10,000 phenolics compounds have been identified in several botanical sources. Structurally, phenolics are compounds with benzene ring/s (C6) attached to hydroxyl group/s (Cn). Phenolics vary depending on having a single or double benzene ring, and the number of carbon chains attached to these rings (Fraga et al., 2010, Tsimogiannis and Oreopoulou, 2019). Simple phenolic compounds such as catechol and hydroquinone contain a single benzene ring with one or two hydroxyl groups attached to different locations. Attachment of a carboxylic acid to benzene ring either directly or through C=C bond results in hydroxybenzoic acids or hydroxycinnamic acids, respectively (e.g., salicylic acid, caffeic acid, etc.). Some phenolics contain two benzene rings linked by one (Xanthonoids), two (stilbenes), or four (lignans) carbon methylene bridges (Al Mamari, 2021, Pandey and Rizvi, 2009, Tsimogiannis and Oreopoulou, 2019). When the two benzene rings (ring A and B) are linked by three carbon atoms that form an oxygenated heterocycle (ring C) flavonoids shape. The variation in number and arrangement of the hydroxyl groups and their extent of alkylation and/or glycosylation on these rings gives rise to seven subclasses of flavonoids (Pandey and Rizvi, 2009, González-Vallinas et al., 2013). There are various approaches for the classification of phytochemicals. For example, they have been categorized based on their plant origin, biological properties, biosynthesis/metabolism, or chemical structure. They are also often classified according to their chemical structure as carotenoids, phenolics, alkaloids, nitrogen-containing compounds, and organosulfur compounds (Liu, 2004).

### 2.1.5. Dietary phytochemicals are drivers of cardiometabolic health

The Mediterranean diet is an example of a healthy diet that is characterized by a high proportion of plant food containing unsaturated fatty acids and phytochemicals (specifical phenolics) (Issaoui et al., 2020, Ditano-Vázquez et al., 2019). The ability of phenolics to act as chemo-preventive agents without harming the healthy tissues opens a new field to study for these phytochemicals. Several fruits and vegetables have been studied to identify and evaluate their phenolics content, bioavailability, and bioactivity. Along with in-vitro studies, many human high phenolic dietary interventions, either as a whole food or as a supplement, have investigated the potential of these compounds to reduce the development of CMD (Tomé-Carneiro and Visioli, 2016). For example, daily supplementation of phenolic extracts has been demonstrated to improve endothelial dysfunction (Barona et al., 2012, Chaves et al., 2009, Engler et al., 2004), reduce inflammatory biomarkers in both healthy and patients with CMD complications, and increase the production of vasodilators, such as nitric oxide (NO) (Loke et al., 2008).

### 2.1.6. Phytochemicals and oxidative stress

One of the important health-promoting functions of phytochemicals is an increase in antioxidant (AOX) activity. Dietary phytochemicals, along with endogenous AOX system, can alleviate the damages inflicted by reactive oxygen and nitrogen species (RONS).

Randomized clinical trials have shown that higher intake of fruits and vegetables results in increased circulation of phytochemicals and improved AOX potential. More specifically, consumption of fruits and vegetables with higher phytochemicals (e.g., phenolics) has been shown to result in an increased plasma AOX capacity (Kountouri et al., 2007, Roussel et al., 2009, Visioli et al., 2005, Record et al., 2001, Lotito and Frei, 2006). Higher plasma AOX capacity results in lower oxidative damage and inflammatory biomarker production and circulation, which is associated with a lower risk of CMD and more specifically cardiovascular disease. Epidemiological, clinical, and experimental studies have provided evidence demonstrating the positive effect of AOX (exogenous or endogenous) on the prevention and improvement of cardiovascular disorders (e.g., myocardial infarction, impaired endothelial dilation).

Preclinical and clinical studies have shown the bioavailability and antioxidant activity of phenolics in plasma after phenolic supplementation (delivered as a water solution) (Mubarak et al., 2012). Supplementation restored endothelial function healthy human and animal models (old and young), as determined by increases in NO-mediated dilation. (Fleenor et al., 2013, Santos-Parker et al., 2017, Vauzour et al., 2010, Turner et al., 2021). Ex-vivo and in-vitro experiments also demonstrated improvements in endothelial function following phenolic supplementation, along with decreased NADPH-dependent superoxide anion levels in hypertensive animal and human arteries (Suzuki et al., 2007, Steffen et al., 2007, Tom et al., 2016). Reduction in the mitochondrial antioxidant enzyme is another feature of aging and arterial dysfunction. Phenolics supplementation has also been demonstrated to increase expression of mitochondrial antioxidant enzyme manganese superoxide dismutase (MnSOD) in old mice to levels not significantly different from young control animals (Fleenor et al., 2013).

Chlorogenic acid (CGA) has been identified as an important phenolic compound that could mediate some of the observed beneficial properties of phenolic supplementation. For example, CGA has been shown to reduce blood pressure in both mice and humans (Suzuki et al., 2002, Suzuki et al., 2007) (Kozuma et al., 2005, Watanabe et al., 2006, Kajikawa et al., 2019, Revuelta-Iniesta and Al-Dujaili, 2014, Castellino et al., 2019, Mubarak et al., 2012). CGA has also been demonstrated to reduce body weight (Cho et al., 2010, Wang et al., 2019b) and improve lipid and glucose homeostasis. Supplementation of CGA improved fasting blood glucose and insulin secretion in patients with impaired glucose tolerance (Zuñiga et al., 2018) and healthy individuals (Katada et al., 2018, Lecoultre et al., 2014). Several other health promoting aspects of CGA have been demonstrated such as antioxidant potential (Yun et al., 2012, Shi et al., 2016, Katada et al., 2018, Victoria-Montesinos et al., 2021) and modification of the gut microbiota (Chen et al., 2019, Shi et al., 2021, Tomas-Barberan et al., 2014).

### 2.1.7. Phenolics: the effect on RAAS and ACE

The effect of phenolics (specifically chlorogenic acid) in cardiovascular health and blood pressure control has also been linked to their ability to reduce components of the RAAS. RAAS inhibitors have been a mainstay for the treatment of cardiovascular and renal diseases for the last 30 years. More recently, the RAAS has become a novel therapeutic target for ophthalmological diseases such as cataracts, glaucoma, diabetic retinopathy, macular degeneration, and uveitis (Patel et al., 2017). As described above, ACE is an important enzyme in the RAAS cascade. ACE inhibitors are among the top forth most commonly used drugs in the United States, after antidepressants, lipid-lowering drugs (at age 40-59) and lipid-lowering, antidiabetic agents and beta-blockers (high blood pressure, heart disease) (age 60-79) (CDC and NCHS, 2019). One of the mechanisms through which phenolics may reduce blood pressure is via ACE inhibition. Phenolics compounds, either as extracts from plant material or pure chemicals, significantly reduced blood pressure in hypertensive rats (Agunloye and Oboh, 2018, Kozuma et al., 2005). This research also revealed that oral gavage of these phenolic compounds significantly reduced ACE activity in the plasma in a dose dependent manner. Ex-vivo studies have shown that phenolic compounds can be released after in vitro digestion and accumulatively exert ACE inhibitory activity (Zieliński et al., 2020, Kozuma et al., 2005, Dalar and Konczak, 2014).

In summary, phenolic compounds have been shown to reduce blood pressure through enhanced antioxidant activity, improvement in systemic inflammation, and inhibition of RAAS.

### 2.1.8. Potatoes and hypertension

The persistent challenge of malnutrition and food-related health issues, such as the development of CMD, has drawn global attention among both politicians and scientists. Further, the consumers' knowledge of healthy eating is improving and the demand for value-added food is on the rise. One of the key aspects of this complex situation is the availability of affordable fruits and vegetables that are not only delivering calories but that also provide health-promoting compounds. Indeed, breeding for nutritionally enhanced crops is increasingly a major focus of agricultural and nutritional research.

As mentioned in chapter one (1.3.), potatoes provide a golden opportunity to improve the nutritional value of the diet and food for the public. Potato germplasm contains a rich gene pool of wild and cultivated varieties, providing breeders an extraordinary chance to develop this crop as a delivery vehicle of health-promoting phytochemicals. Five market classes of potato have been introduced by breeders, defined mostly by phenotypic properties of the tubers (Russet, Yellow, Red, Chipper, and Specialty).

Previous studies have characterized variation among different genotypes in their bioactive compounds including phytochemicals, minerals, vitamins, and proteins/amino acids. A recent comprehensive non-targeted metabolomics study revealed that 53% of all detected compounds in cooked potatoes varied among market classes (Chaparro et al., 2018). Also, the differences in protein content and amino acid (AA) composition among different potato market classes and based on their cooking status has been reported (Pęksa et al., 2013, Pinhero et al., 2016). In-vitro antioxidant measurements of small molecule extracts of different potato genotypes show significant variation among various genotypes. For example, a comparison of antioxidant activity between purple and white varieties showed purple potato had higher AOX (Tsang et al., 2018).

The consumption of potato varieties that are higher in phytochemicals (e.g., phenolics) has been linked to improvement in CMD risk factors. Tsang et al., conducted small-scale intervention study to assess the effect of daily consumption of high phenolic potatoes compared to low phenolic cultivars in healthy adults (Tsang et al., 2018). Their results showed that daily consumption of 200 grams of the high phenolic cultivar improved pulse wave velocity (a measure of arterial stiffness) in healthy males and females compared to the low phenolic white cultivar. In conjunction with these results, protein extract from both a white cultivar (Lady Christl) and a yellow cultivar (Asterix) showed ACE inhibitory activity in-vitro (Pihlanto et al., 2008, Makinen et al., 2008, Mäkinen et al., 2016).

Previous research has demonstrated ACE inhibitory activity of phenolic compounds extracted from different plant source such as soybeans, legumes, buckwheat, cowpeas, citrus, and grapes (Ademiluyi and Oboh, 2013, Mamilla and Mishra, 2017, Zieliński et al., 2020, Irondi et al., 2019, Ruviaro et al., 2020, López-Fernández-Sobrino et al., 2021, Dwibedi et al., 2022). This suggests that similar phenolics (e.g., chlorogenic acid) in potato would demonstrate similar activity. However, to our knowledge there is no evidence demonstrating ACE inhibitory activity of phenolics isolated from potatoes. Furthermore, based on previous research demonstrating significant variation in metabolite composition between potato advanced line and cultivars (Chaparro et al., 2018, Bártová et al., 2015, Subramanian et al., 2017, Andre et al., 2007b) we hypothesize that this variation could be leveraged to enable breeding of potato cultivars with improved health promoting attributes. Potatoes are a cheap, widely consumed, sustainable crop that is a great candidate to obtain these phytochemicals through diet.

A knowledge gap remains in our understanding of the variation in composition and bioactivity of small molecules across potato genotypes and market classes. I hypothesize that that genotype variation will correlate with phytochemical composition and bioactivity. This hypothesis I tested in the following three objectives:

1) characterization of the phenolic composition of 60 potato genotypes

2) quantification of chlorogenic acid in 25 potato genotypes and

3) evaluation of ACE inhibitory activity in a low and a high phenolic potato cultivar.

## 2.2. Experimental Procedure

### 2.2.1. Chemicals and solvents

Angiotensin converting enzyme from rabbit lung (ACE), Captopril, hippuric acid (HA), chlorogenic acid, folin–ciocalteu's reagent, and sodium carbonate (Na2CO3) were purchased from SIGMA (Millipore Sigma, USA). UPLC grade Methanol, $H_2O$, Acetonitrile purchased from Fisher (Thermo Fisher Scientific, USA).

### 2.2.2. Plant material

Potatoes were provided by the Colorado State University Potato Breeding and Selection Program in 2014 and 2015. In total, we were provided 57 advanced selections and named genotypes in 2014 and 24 advanced selections and named cultivars in 2015 spanning multiple market classes (russets, reds, yellows, chippers, and specialties) with six biological replicates per genotype. Potatoes were washed under tap water to make sure there was no soil residue left on the skin, then rinsed under distilled water. The tubers were divided into two groups, each with three biological replicates. Potatoes in group one was processed raw (2014 only), and potatoes in group two were processed after cooking (2014 and 2015). The tubers were cooked using methods previously established in our laboratory by Chapparo et al., (Chaparro et al., 2018). Briefly, the fresh weight of each potato was used to calculate cooking time, where 30 g of potato fresh weight was cooked using a microwave for 1.75 min at 400 W power. After cooking, potato tubers were immediately frozen in liquid nitrogen. and kept in -80 C. The frozen raw and cooked potato tuber samples were shattered using a hammer and freeze-dried. The freeze-dried samples were ground into powder using coffee grinder (Krups, krupsusa.com). The fine powders were kept at -20°C until analysis.

### 2.2.3. Small molecules extraction, Phenolics/ AOX measurement

Fifty milligrams of each potato sample (cooked and raw, each with 3 biological replicates) was weighted in a 2mL eppendorf tube. To extract the small molecules or total phenol, 1000 µL of 80 % v/v (Methanol: water) was added to each tube. All tubes were vortexed for an hour at 4°C, on a horizontal shaker. The samples were then centrifuged (8000 g for 20 min at 4°C). The liquid supernatant was collected from all tubes and dried under liquid nitrogen. The dried samples were resuspended in 50% methanol: water and stored at -20°C until further analysis.

The folin–ciocalteau method (FC) method (Obanda et al., 1997) was used to evaluate the phenolic quantity in these genotypes. The FC method has also been used as an indicator of AOX activity (Prior et al., 2005, López-Froilán et al., 2018, Derakhshan et al., 2018). A calibration curve of gallic acid (ranging from 0.01 to 500 µg/ml) was prepared, and the results were expressed as mg gallic acid equivalents per gram of the sample. The FC reagent was diluted 1:9 with water and 450 ul was added to 105 ul of each sample. A 450 µl of FC and water mixture were added to 105 µl of samples. The sample was incubated in the dark at room temperature (24°C) for 10 minutes, then 340 µl of 7% v/v Sodium Carbonate (NaCO3) with water was added to each tube and vortexed for 10 seconds. The sample was again incubated in the dark at room temperature (24°C) for 30 more minutes. 100 µl of each sample was added to a 96 plate, with 3 replicates for each sample. The absorbance was measured by a spectrophotometer at 765 nm.

### 2.2.4. Quantification of chlorogenic acid (CGA) in potato genotypes.

The cooked potato powder was prepared and extracted as described above. A series of CGA standards were prepared in 80% v/v methanol/water. All extracts and standards were analyzed using an BioAcquity H-Class UPLC coupled to a Photodiode Array (PDA) detector with separation using a Waters Acquity UPLC BEH C18 column (1.7 µM, 2.1 x 50 mm). The injection volume was 10 µl, the flow rate was 0.5 ml/min with a gradient of acetonitrile in 0.1% TFA (20-90%) and water (80-10%) in 15 minutes, and the detection was monitored at 328 nm.

### 2.2.5. Determination of ACE-inhibitory activity using UPLC

We used the method described by Pihlanto (Pihlanto et al., 2008) with modification. Briefly, 100 µl of hippuryl-l-histidyl-l-leucine (HHL) solution (5 mM in 0.1 M borate buffer pH 8.3, containing 0.4 M NaCl) were incubated with 10 µl of sample (phenolic extracts, Captopril or chlorogenic acid) at 37°C for 15 min. After incubation, the ACE enzyme (20 µL of 100 mU enzyme) was added to the sample/substrate mixture and the kinetic reaction started, the mixtures were incubated for another 30 min. The reaction was stopped with 20 µl of 5 M HCl. The hippuric acid liberated by ACE was measured by BioAcquity H-Class UPLC coupled to a Photodiode Array (PDA) detector, and separation was performed using a Waters Acquity UPLC BEH C18 column (1.7 µM, 2.1 x 50 mm). The injection volume was 10 µl, the flow rate was 0.5 ml/min with a gradient of acetonitrile (100%) and water (80-10%) in 15 minutes, and the effluent was monitored at 228 nm. All injunctions were carried out in duplicate. The ACE-inhibitory activity was calculated according to the following equation: Inhibitory activity (%) = [(HAcontrol −

HAsample)/HAcontrol] × 100%. The determinations were carried out in duplicate. The positive control for ACE inhibition was Captopril (N-[(S)-3-mercapto-2-methylpropionyl]-L-proline).

### 2.2.6. Statistical analysis

All statistical analysis was performed with GraphPad Prism version 9 (GraphPad Software, USA, California). Data are presented as mean ± standard error of the mean (SE). Significance was considered with a *P-value* of $< 0.05$. One-way ANOVA with Tukey's post hoc test was used for variables measured within and between the market classes. We used Log10 transformation to normalize the data when data did not pass tests for normality. A student t-tests with multiple comparison testing using the Benjamini, Krieger, and Yekutieli two-stage step-up method used to compare paired cooked and raw samples.

## 2.3. Results

### 2.3.1. Variation in small molecules quantity and AOX activity among different potato genotypes.

This experiment was performed on potato tubers provided by the CSU potato breeding program in 2014 and represents a set of 57 genotypes within five different market classes. Statistically significant variation in phenolic content of cooked tubers was observed between the Specialty market class compared to Russet, Chippers, Red, and Yellow (Figure 2.1, Table 2.1). Notably, the highest phenolic content was observed in the Specialty market class.

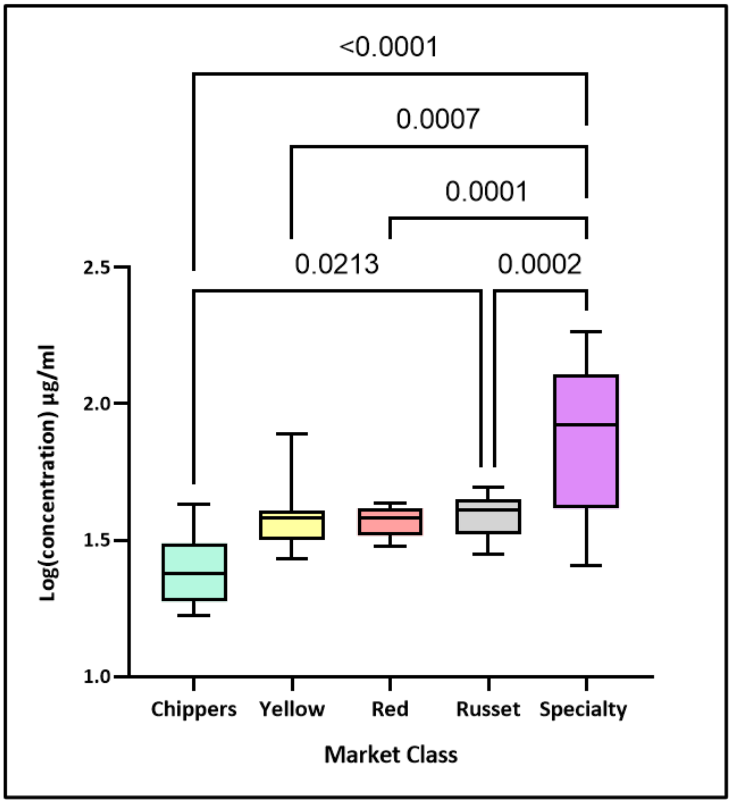


**Figure 2.1.** Total phenolic content of cooked tubers for each market class. Data are expressed as the mean ± SE; n=3 tubers/genotype. Statistical analysis was performed between market classes on log transformed data using a one-way ANOVA with Tukey's post hoc test.

Variation in phenolic content for cooked tubers was also observed within each market class (Figure 2.2). Selected genotypes within the Russet and Red market classes varied, though these differences were not statistically significant. Within the Russet market class, the highest phenolic content was observed in the cultivar Mesa Russet (49.56 ± 4.01 mg/mL) and the lowest was in Fortress Russet (28.1 ± 0.21 mg/mL). Within the Red market class, the highest phenolic content was observed in the cultivar Rio Colorado (43.71 ± 6.17) and the lowest was in Colorado Rose (30.00 ± 1.67). The variation in phenolic content within in the Chippers, Yellow, and Specialty market classes were statistically significant (Figures 2.2. and 2.3, Table 2.1).

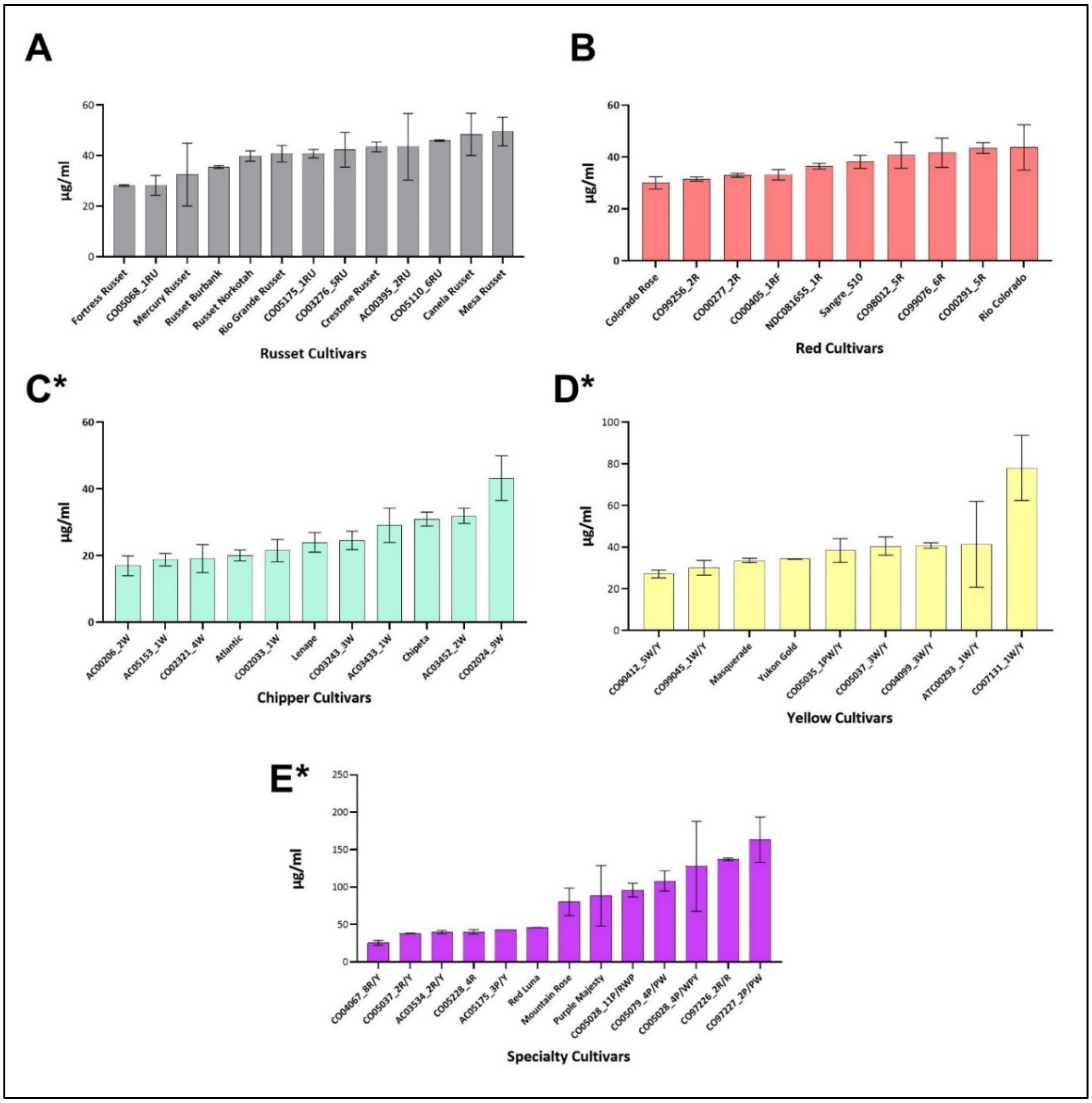


**Figure 2.2.** Total phenolic content of cooked tubers from genotypes within each market class. A) Russet B) Red C) Yellow D) Chippers E) Specialty. Data are expressed as the mean $\pm$ SE; n=3 tubers/genotypes. The starred graphs (C, D, and E) represent the market classes with statistically significant variation within the genotypes (see Figure 2.3). Statistical analysis was performed between genotypes within each market classes using a one-way ANOVA with Tukey's post hoc test.

A

| Chippers Cultivars | AC05153_1W | CO02321_4W | Atlantic | CO02033_1W | Lenape | CO03243_3W | AC03433_1W | Chipeta | AC03452_2W | CO02024_9W |
|---|---|---|---|---|---|---|---|---|---|---|
| AC00206_2W | >0.9999 | 0.9998 | 0.997 | 0.9569 | 0.6765 | 0.5852 | 0.1176 | 0.0545 | 0.036 | 0.0005 |
| AC05153_1W | | >0.9999 | >0.9999 | 0.999 | 0.9127 | 0.8515 | 0.2441 | 0.1179 | 0.0786 | 0.0009 |
| CO02321_4W | | | >0.9999 | 0.9997 | 0.9393 | 0.8882 | 0.2764 | 0.1351 | 0.0904 | 0.001 |
| Atlantic | | | | >0.9999 | 0.983 | 0.9585 | 0.3789 | 0.1932 | 0.1308 | 0.0014 |
| CO02033_1W | | | | | 0.9995 | 0.9972 | 0.5864 | 0.3313 | 0.2318 | 0.0024 |
| Lenape | | | | | | >0.9999 | 0.9152 | 0.6818 | 0.5316 | 0.0062 |
| CO03243_3W | | | | | | | 0.9574 | 0.7693 | 0.6223 | 0.0079 |
| AC03433_1W | | | | | | | | >0.9999 | 0.9985 | 0.052 |
| Chipeta | | | | | | | | | >0.9999 | 0.1123 |
| AC03452_2W | | | | | | | | | | 0.1668 |

B

| Yellow Cultivars | CO99045_1W/Y | Masquerade | Yukon Gold | CO05035_1PW/Y | CO05037_3W/Y | CO04099_3W/Y | ATC00293 _1W/Y | CO07131_1W/Y |
|---|---|---|---|---|---|---|---|---|
| CO00412_5W/Y | >0.9999 | 0.9968 | 0.994 | 0.9233 | 0.8407 | 0.8293 | 0.7983 | 0.0058 |
| CO99045_1W/Y | | >0.9999 | 0.9999 | 0.9854 | 0.9502 | 0.9441 | 0.9264 | 0.0087 |
| Masquerade | | | >0.9999 | 0.9996 | 0.9957 | 0.9946 | 0.9909 | 0.0143 |
| Yukon Gold | | | | 0.9999 | 0.9978 | 0.9972 | 0.9948 | 0.0157 |
| CO05035_1PW/Y | | | | | >0.9999 | >0.9999 | >0.9999 | 0.0286 |
| CO05037_3W/Y | | | | | | >0.9999 | >0.9999 | 0.0388 |
| CO04099_3W/Y | | | | | | | >0.9999 | 0.0402 |
| ATC00293 _1W/Y | | | | | | | | 0.0441 |

C

| Specialty Cultivars | CO05037_2R/Y | AC03534_2R/Y | AC05175_3P/Y | Red Luna | Mountain Rose | Purple Majesty | CO05028_11P/RWP | CO05079_4P/PW | CO05028_4P/WPY | CO97226_2R/R | CO97227_2P/PW | CO04063_4R/R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CO04067_8R/Y | >0.9999 | >0.9999 | 0.9998 | 0.9992 | 0.5623 | 0.3851 | 0.2552 | 0.1199 | 0.0323 | 0.0171 | 0.0029 | 0.0007 |
| CO05037_2R/Y | | >0.9999 | >0.9999 | >0.9999 | 0.8391 | 0.6655 | 0.4912 | 0.2595 | 0.0755 | 0.0404 | 0.0067 | 0.0015 |
| AC03534_2R/Y | | | >0.9999 | >0.9999 | 0.8696 | 0.7059 | 0.5309 | 0.2867 | 0.0848 | 0.0455 | 0.0075 | 0.0017 |
| AC05175_3P/Y | | | | >0.9999 | 0.9186 | 0.7797 | 0.6093 | 0.3448 | 0.1059 | 0.0571 | 0.0095 | 0.0021 |
| Red Luna | | | | | 0.9496 | 0.8356 | 0.6755 | 0.3993 | 0.1272 | 0.0691 | 0.0115 | 0.0025 |
| Mountain Rose | | | | | | >0.9999 | >0.9999 | 0.9889 | 0.7374 | 0.5227 | 0.1186 | 0.026 |
| Purple Majesty | | | | | | | >0.9999 | 0.9994 | 0.8916 | 0.7119 | 0.1978 | 0.0454 |
| CO05028_11P/RWP | | | | | | | | >0.9999 | 0.9708 | 0.8636 | 0.3063 | 0.0753 |
| CO05079_4P/PW | | | | | | | | | 0.9995 | 0.9857 | 0.5583 | 0.1667 |
| CO05028_4P/WPY | | | | | | | | | | >0.9999 | 0.9389 | 0.4903 |
| CO97226_2R/R | | | | | | | | | | | 0.9929 | 0.7051 |
| CO97227_2P/PW | | | | | | | | | | | | 0.9981 |

**Figure 2.3.** *P-values* for all genotype pairs within each market class. A) Chippers B) Yellow C) Specialty (no significant *P-values* were observed for any genotype pairs within the Red or Russet market classes). Statistical analysis was performed between genotypes within each market class using a one-way ANOVA with Tukey's post hoc test.

Several previous studies have reported that the results of the FC test (used here to determine phenolic content) are also representative of AOX potential. This provides us with an opportunity to evaluate if cooking has an impact on the AOX potential - which is important given that potatoes are not consumed raw. No significant differences in AOX potential between raw and cooked potatoes were observed for any of the genotypes (Figure 2.4, Table 2.1).

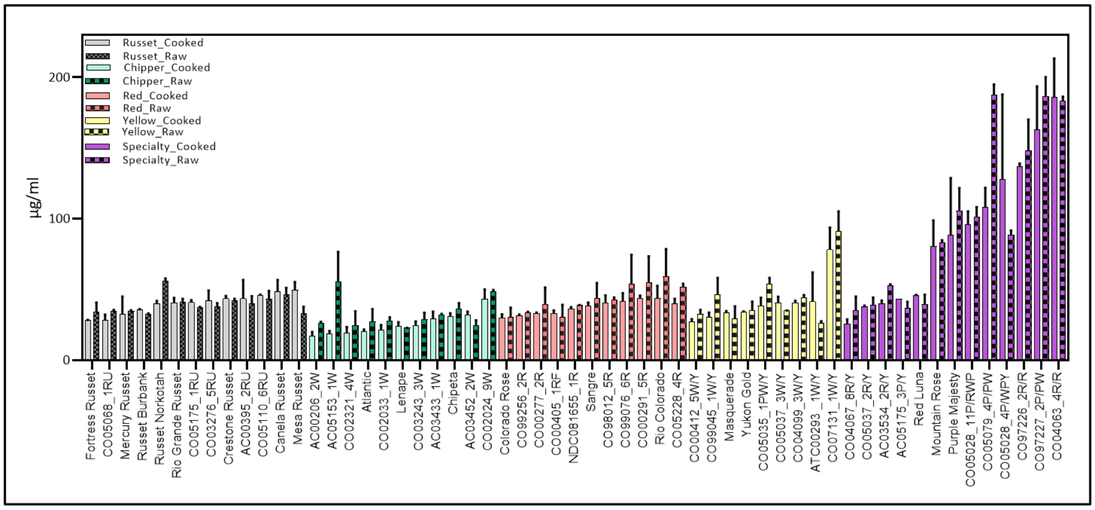


**Figure 2.4**. AOX potential of raw and cooked potatoes. Data are expressed as the mean ± SE; n=3 tubbers/genotype. Statistical analysis was performed between raw and cooked tubers for each genotype using a student t-tests with multiple comparison testing using the Benjamini, Krieger, and Yekutieli two-stage step-up method. No significant comparisons were observed between cooked and raw.

**Table 2.1.** Total phenolics (AOX potential) for all genotypes in each market class (cooked and raw) as measured by the FC test.

| Market Class | Genotype | Cooked (µg/mL) | Raw (µg/mL) | Market Class (µg/mL) |
|---|---|---|---|---|
| Russet | CO05068_1RU | 28.2 ± 2.8 | 34.6 ± 0.6 | 39.9 ± 1.9 |
| | Mercury Russet | 32.5 ± 8.8 | 34.6 ± 0.4 | |
| | Russet Burbank | 35.5 ± 0.4 | 32.3 ± 0.4 | |
| | Russet Norkotah | 39.8 ± 1.4 | 56. ± 1.2 | |
| | Rio Grande Russet | 40.7 ± 2.3 | 41.2 ± 1.5 | |
| | CO05175_1RU | 40.7 ± 1.2 | 37.4 ± 0.1 | |
| | CO03276_5RU | 42.3 ± 4.8 | 37.7 ± 1.8 | |
| | Crestone Russet | 43.4 ± 1.3 | 42.2 ± 0.9 | |
| | AC00395_2RU | 43.4 ± 9.3 | 39.7 ± 3.9 | |
| | CO05110_6RU | 46. ± 0.2 | 43.2 ± 4. | |
| | Canela Russet | 48.4 ± 5.9 | 46.1 ± 3.5 | |
| | Mesa Russet | 49.6 ± 4. | 33.2 ± 3.2 | |
| Chippers | AC00206_2W | 16.9 ± 2.1 | 26. ± 0.8 | 25.4 ± 2.4 |
| | AC05153_1W | 18.8 ± 1.3 | 55.2 ± 15.1 | |
| | CO02321_4W | 19.1 ± 3. | 24.6 ± 7. | |

| | | | | |
|---|---|---|---|---|
| | Atlantic | 20. ± 1.2 | 27. ± 6.3 | |
| | CO02033_1W | 21.5 ± 2.4 | 27.9 ± 1.6 | |
| | Lenape | 23.9 ± 2.1 | 22.8 ± 0.1 | |
| | CO03243_3W | 24.5 ± 2. | 28.7 ± 3.4 | |
| | AC03433_1W | 29.1 ± 3.6 | 31.7 ± 0.7 | |
| | Chipeta | 30.9 ± 1.5 | 36.1 ± 3. | |
| | AC03452_2W | 31.9 ± 1.6 | 24.5 ± 2.6 | |
| | CO02024_9W | 43.2 ± 4.8 | 48.6 ± 0.7 | |
| | Colorado Rose | 30. ± 1.7 | 30.6 ± 4.5 | |
| | CO99256_2R | 31.5 ± 0.5 | 33.7 ± 0.3 | |
| | CO00277_2R | 32.9 ± 0.5 | 39.5 ± 8.4 | |
| | CO00405_1RF | 33.2 ± 1.4 | 30.3 ± 6.1 | |
| | NDC081655_1R | 36.4 ± 0.8 | 38.8 ± 0.1 | |
| Red | Sangre | 38.2 ± 1.8 | 43.5 ± 7.8 | 37.4 ± 1.5 |
| | CO05228_4R | 40.2 ± 2.2 | 51.6 ± 1.7 | |
| | CO98012_5R | 40.7 ± 3.5 | 42.9 ± 1. | |
| | CO99076_6R | 41.7 ± 4. | 54. ± 14.5 | |
| | CO00291_5R | 43.5 ± 1.5 | 55. ± 13. | |
| | Rio Colorado | 43.7 ± 6.2 | 59.1 ± 13.7 | |
| | CO00412_5W/Y | 27.1 ± 1.3 | 32.6 ± 2. | |
| | CO99045_1W/Y | 30.1 ± 2.5 | 46.2 ± 8.4 | |
| | Masquerade | 33.6 ± 0.7 | 29.1 ± 6.3 | |
| | Yukon Gold | 34.3 ± 0.1 | 35.4 ± 4.2 | |
| Yellow | CO05035_1PW/Y | 38.4 ± 4. | 53.6 ± 3.2 | 40.5 ± 5. |
| | CO05037_3W/Y | 40.5 ± 3.1 | 34.9 ± 0.1 | |
| | CO04099_3W/Y | 40.7 ± 0.9 | 44.1 ± 1.3 | |
| | ATC00293 _1W/Y | 41.3 ± 14.6 | 25.8 ± 1.1 | |
| | CO07131_1W/Y | 78.1 ± 11.1 | 91.2 ± 9.9 | |
| | CO04067_8R/Y | 25.6 ± 2.3 | 35. ± 7.1 | |
| | CO05037_2R/Y | 38.1 ± 0.4 | 39. ± 3.7 | |
| | AC03534_2R/Y | 39.8 ± 1.6 | 52.5 ± 0.7 | |
| | AC05175_3P/Y | 43.2 ± 0. | 36.5 ± 3.3 | |
| Specialty | Red Luna | 46. ± 0.1 | 39.4 ± 4.8 | 90.7 ± 14.4 |
| | Mountain Rose | 80.4 ± 13. | 83.1 ± 1.3 | |
| | Purple Majesty | 88.5 ± 28.5 | 105.5 ± 11.5 | |
| | CO05028_11P/RWP | 96. ± 6.5 | 101.5 ± 4.8 | |

| | | | |
|---|---|---|---|
| | CO05079_4P/PW | 108.2 ± 9.7 | 187.4 ± 5.3 |
| | CO05028_4P/WPY | 127.7 ± 42.5 | 88.4 ± 2.4 |
| | CO97226_2R/R | 137. ± 1.4 | 148.2 ± 15.6 |
| | CO97227_2P/PW | 163.3 ± 21.4 | 186.7 ± 9.5 |
| | CO04063_4R/R | 185.7 ± 19.5 | 183.5 ± 2. |

Data expressed as mean ± SE; n= 3 tubers/genotypes.

### 2.3.2. Chlorogenic acid in potato tubers

As mentioned in section 2.1.6., chlorogenic acid (CGA) is an important phenolic that has been demonstrated to have several therapeutic benefits in both experimental and clinical trials. Thus, in addition to total phenolic content, we measured the specific concentration of CGA. This experiment was performed on potato tubers provided by the CSU Potato Breeding Program in 2015 and represents a different set of 24 genotypes spanning the five market classes. The CGA content of tubers was measured using UPLC (Figure 2.5., Table 2.2.). Overall, the highest CGA content was measured in the Specialty market class (64.36 ± 11.80 µg/mL).

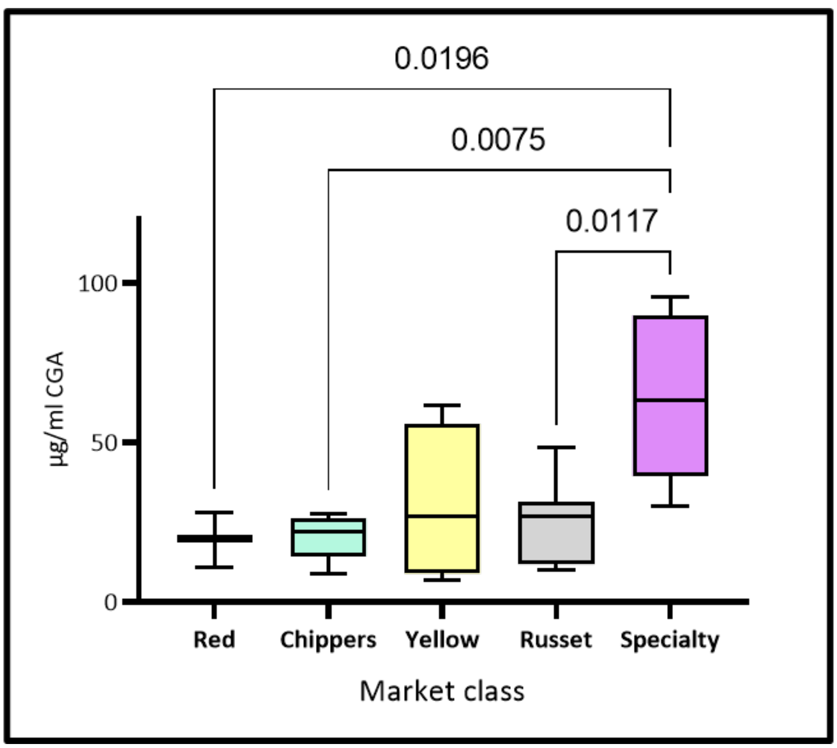

**Figure 2.5.** Chlorogenic acid content of cooked tubers for each market class. Data are expressed as the mean ± SE; n= 3 tubers/genotypes. Statistical analysis was performed using a one-way ANOVA with Tukey's post hoc test.

Variation in CGA content in cooked tubers was also observed within each market class. Selected genotypes within the Russet, Yellow, Chippers, Specialty and Red market classes varied with statistically significant differences among some genotypes (Figure 2.6). For example, within the Russet market class, CO07015_4RU (48.52 ± 4.6 µg/mL) had significantly higher CGA content compared to CO07049_1RU (10.28 ± 3.4 µg/mL), CO08231_1RU (11.86 ± 5.4 µg/mL), and Rio Grande Russet (23 ± 0.8 µg/mL). In the Yellow market class, we observed a 159% difference in CGA content between the CO07131_1W_Y (highest,61.7 ± 4.1 µg/mL) and Yukon Gold (lowest, 6.9 ± 0.6 µg/mL). In the Chippers market class, Atlantic had the lowest CGA content compared to 4 other genotypes. In the Red market class, the CGA content in NDC081655_1R, was significantly higher (28.2 ± 4.4 µg/mL) compared to Colorado Rose (10.8 ± 2.1 µg/mL). In the Specialty class we observed a statistically significant difference between TC05276_7P_PW (95.8 ± 7.4 µg/mL) and CO07329_1P_Y (30.2 ± 4.2 µg/mL).

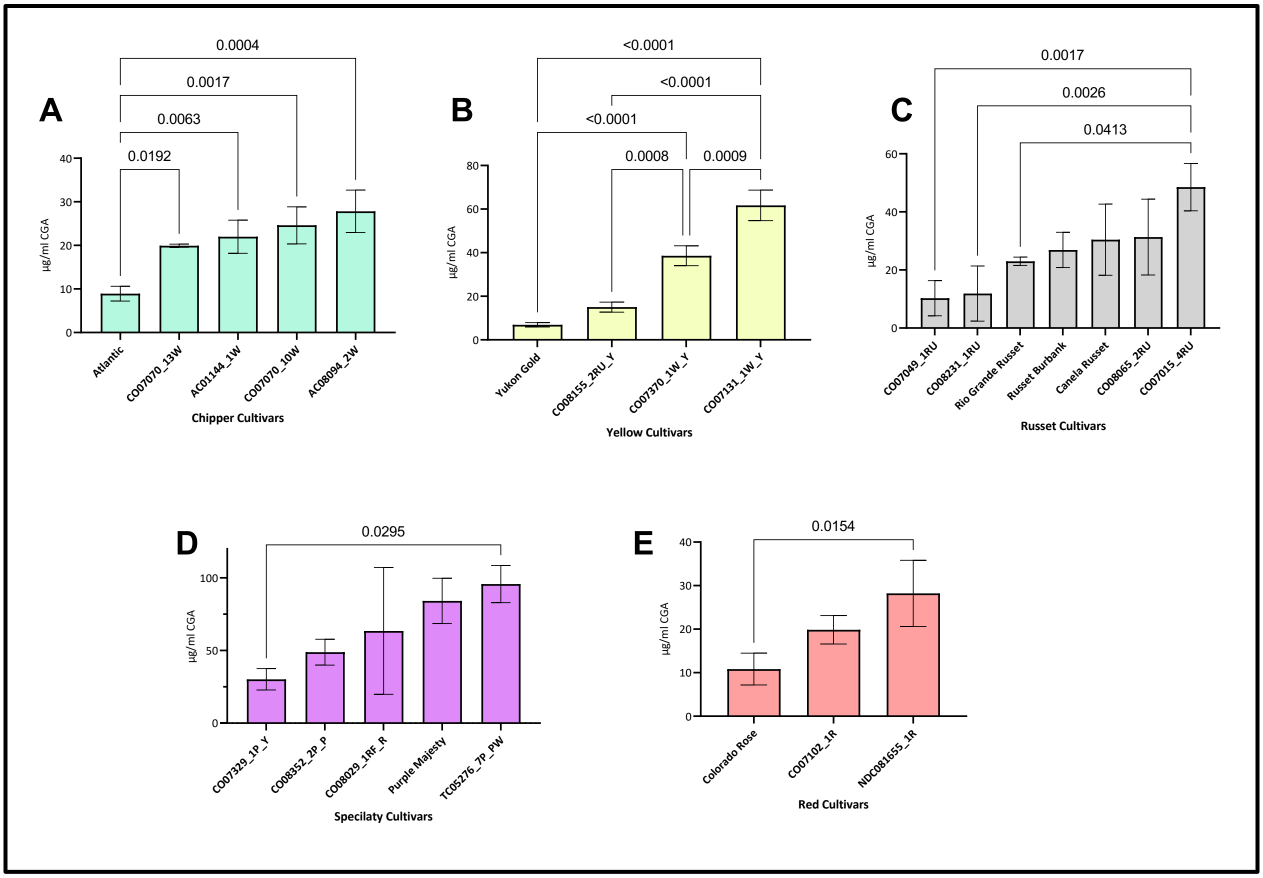


**Figure 2.6.** Chlorogenic acid content from cooked tubers from genotypes within each market class. A) Chippers B) Yellow C) Russet D) Specialty E) Red. Data are expressed as the mean ± SE; n=3 tubers/genotypes. Statistical analysis was performed between genotypes within each market classes using a one-way ANOVA with Tukey's post hoc test.

Overall, the highest chlorogenic acid content was detected in TC05276_7P_PW (95.75 ± 7.3 µg/mL) in the Specialty market class and the lowest CGA content was detected in Yukon Gold (7.0 ± 0.6 µg/mL) in the Yellow market class. However, the story is different when evaluating the ratio of CGA to the total phenolic content. This analysis revealed that the highest %CGA was detected in Midnight Moon (47%), Canela Russet (35%), and Russet Burbank (31%). The fact that two of the high %CGA genotypes are from the Russet market class is an important finding. These represent highly produced and consumed white potato varieties and thus this result demonstrates the potential for development of nutritionally beneficial high CGA genotypes withing this consumer accepted market class.

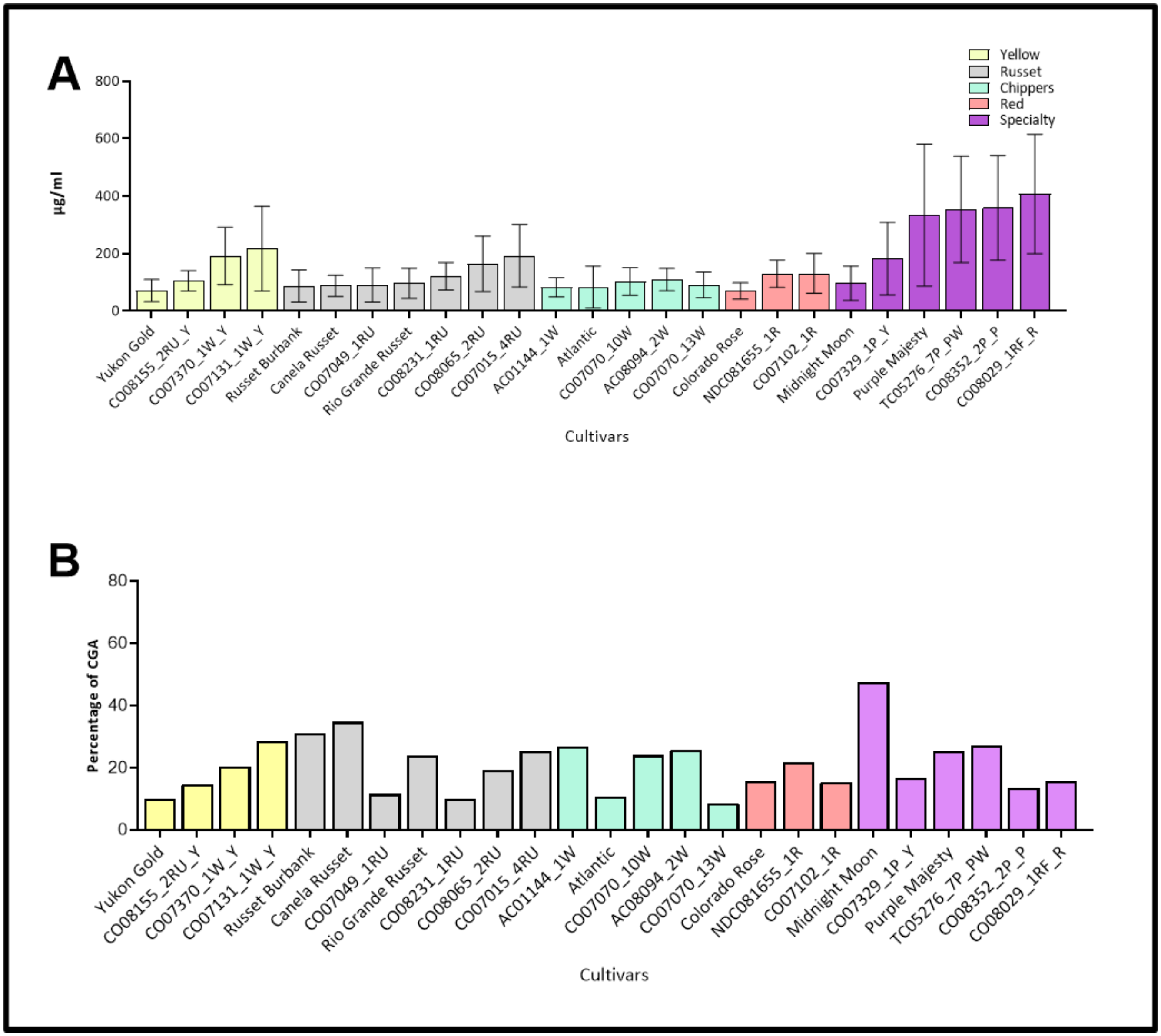


**Figure 2.7.** A) Total phenolic content of cooked tubers from genotypes from different market classes. Data are expressed as the mean ± SE; n=3 tubers/genotypes. B) The percentage of chlorogenic acid relative to total phenolic content in different genotypes.

**Table 2.2.** Total phenolic and CGA content of cooked tubers.

| Market Class | Cultivar | Total Phenolic (ug/mL) | CGA (ug/mL) | % of total phenolics represented by CGA |
|---|---|---|---|---|
| Yellow | Yukon Gold | 70.3 ± 22.5 | 6.9 ± 0.6 | 9.8 |
| | CO08155_2RU_Y | 104.1 ± 20.6 | 15. ± 1.3 | 14.4 |
| | CO07370_1W_Y | 191.3 ± 57.7 | 38.6 ± 2.6 | 20.2 |
| | CO07131_1W_Y | 216.5 ± 85.5 | 61.7 ± 4.1 | 28.5 |
| Russet | CO07049_1RU | 89.5 ± 34.3 | 10.3 ± 3.5 | 11.5 |
| | CO08231_1RU | 120.2 ± 27.7 | 11.9 ± 5.5 | 9.9 |
| | Rio Grande Russet | 96.3 ± 30.4 | 23. ± 0.8 | 23.9 |
| | Russet Burbank | 86.6 ± 32.4 | 26.9 ± 3.5 | 31.1 |
| | Canela Russet | 87.5 ± 21.1 | 30.4 ± 7.1 | 34.8 |
| | CO08065_2RU | 164. ± 55.8 | 31.3 ± 7.5 | 19.1 |
| | CO07015_4RU | 191.4 ± 62.8 | 48.5 ± 4.7 | 25.3 |
| Chippers | Atlantic | 83.2 ± 42.4 | 8.9 ± 1. | 10.7 |
| | CO07070_13W | 232.1 ± 142.6 | 19.9 ± 0.2 | 8.6 |
| | AC01144_1W | 81.8 ± 19.4 | 22. ± 2.2 | 26.9 |
| | CO07070_10W | 102.4 ± 27.4 | 24.6 ± 2.5 | 24.0 |
| | AC08094_2W | 108.8 ± 22.7 | 27.8 ± 2.8 | 25.6 |
| Red | Colorado Rose | 69.1 ± 16.6 | 10.8 ± 2.1 | 15.7 |
| | CO07102_1R | 130. ± 40.1 | 19.8 ± 1.9 | 15.3 |
| | NDC081655_1R | 129.1 ± 27.7 | 28.2 ± 4.4 | 21.9 |
| Specialty | CO07329_1P_Y | 181.7 ± 72.8 | 30.2 ± 4.2 | 16.6 |
| | Midnight Moon | 96.3 ± 34.6 | 45.7 ± 27.7 | 47.5 |
| | CO08352_2P_P | 358.5 ± 105.3 | 48.9 ± 5.1 | 13.6 |
| | CO08029_1RF_R | 406.5 ± 120. | 63.5 ± 25.2 | 15.6 |
| | Purple Majesty | 333.1 ± 142.4 | 84.1 ± 9. | 25.3 |
| | TC05276_7P_PW | 353.2 ± 106.9 | 95.8 ± 7.4 | 27.1 |

Data expressed as mean ± SE; n=3 tubers/genotypes. The percentage of

### 2.3.3. The ACE inhibitory potential of potato small molecules

We established a high-throughput in-vitro system to measure the ACE inhibitory activity of small molecules extracted from potato tubers. To optimize our assay, we first needed to establish the substrate Hippuryl Histidyl Leucine (HHL) concentration and incubation time between the substrate and enzyme Angiotensin Converting Enzyme (ACE) that would result in the highest concentration of the product Hippuric Acid (HA). Our results demonstrated that there was no difference in HA production after 30 minutes, and 7 mg/ml of HHL was found to be the optimum substrate concentration (Figure 2.8).

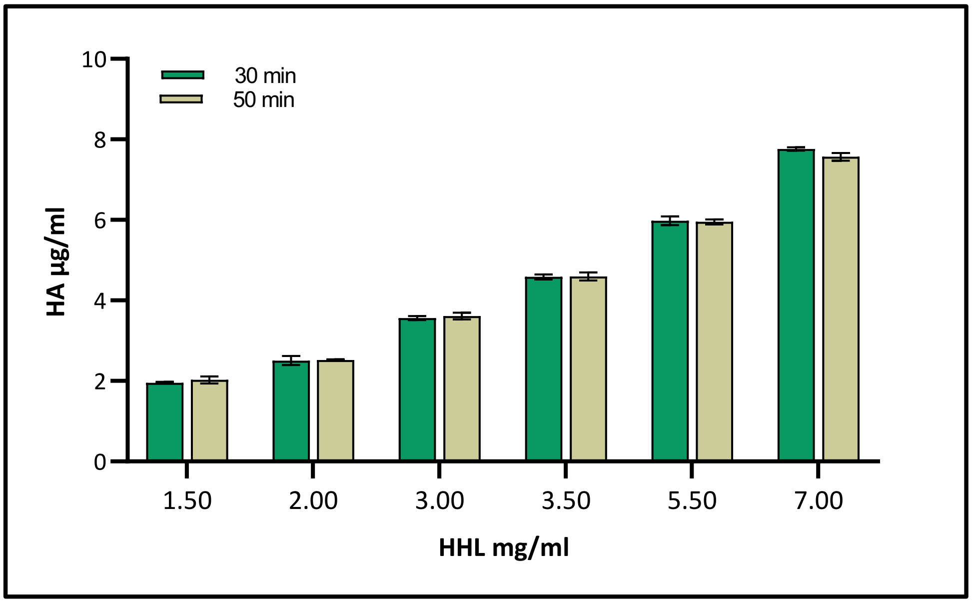


**Figure 2.8.** Optimization of assay parameters for measurement of Hippuric Acid (HA) production in vitro. Increasing the incubation time from 30 to 60 minutes did not increase the HA production. Maximum HA detection was observed using and HHL concentration of 7 mg/ml. Data are expressed as the mean ± SE; n=4.

The next step of the assay optimization was to confirm ACE inhibition activity of two selected positive controls, Captopril and chlorogenic acid (CGA). Captopril, a peptide derivative, is the FDA approved medication used to inhibit ACE in humans and has been used as a positive control in several in vitro studies (López-Fernández-Sobrino et al., 2021, Miguel et al., 2009). Numerous in vivo (Agunloye et al., 2019, Huang et al., 2017, Pihlanto et al., 2008, Mäkinen et al., 2016) and in vitro (Agunloye and Oboh, 2018, Wang et al., 2021, Geng et al., 2010) studies have demonstrated ACE inhibitory activity of CGA supporting our choice of this compound as an additional positive control that represents a naturally derived phenolic. In this assay, ACE inhibitory activity is reflected by a decrease in detected HA. Thus, we would expect to observe an inverse relationship between the concentration of the positive controls and HA. As demonstrated in Figure 2.9. both captopril and CGA reduced the activity of ACE in vitro.

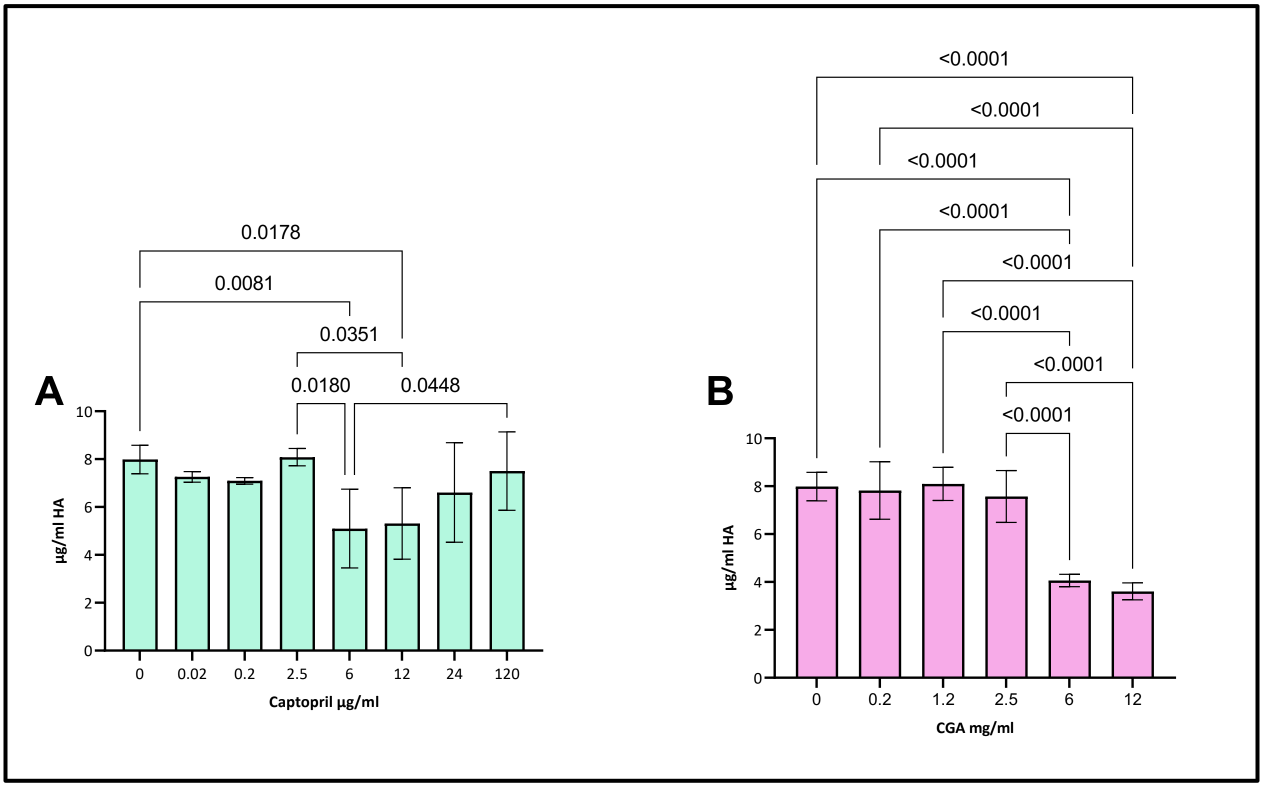


**Figure 2.9.** ACE inhibitory activity of CGA and Captopril in-vitro. Data are represented as µg/ml HA production after 30 minutes in presence of CGA and captopril. Statistical analysis was performed using a one-way ANOVA with Tukey's post hoc test. Data expressed as mean ± SE; n=6/group.

Small molecules were extracted from two phenotypically distinct cultivars of two different market classes to evaluate their ACE inhibitory potential. Purple Majesty (PM) was selected as a representative of cultivars with high phenolics and CGA content, and Canela Russet was selected to represent a conventional white variety with low phenolics and CGA content. While both cultivars showed ACE inhibitory potential in this in vitro assay, PM demonstrated the highest inhibitory activity ($P < .01$) (Figure 2.10 C). Specifically, a 100 µl extract from PM inhibited ACE by 82% compared to control (the control contained no inhibitors), whereas the same volume extract from CR reduced the ACE activity by only 36%. The 100 µl of the PM and CR contained 20 and 13 µg/ml total phenolic content, respectively. For both cultivars, a dose-dependent inhibitory effect was observed (e.g., increasing extract volume resulted in an increase in ACE inhibition reflected by a decrease in HA concentration, Figure 2.10 A and B). These results strongly suggest that ACE inhibition is related to the phenolic content in potato. However, we know other compounds (such as amino acids) can also inhibit ACE and we can not exclude the influence of another compound co-extracted with phenolics.

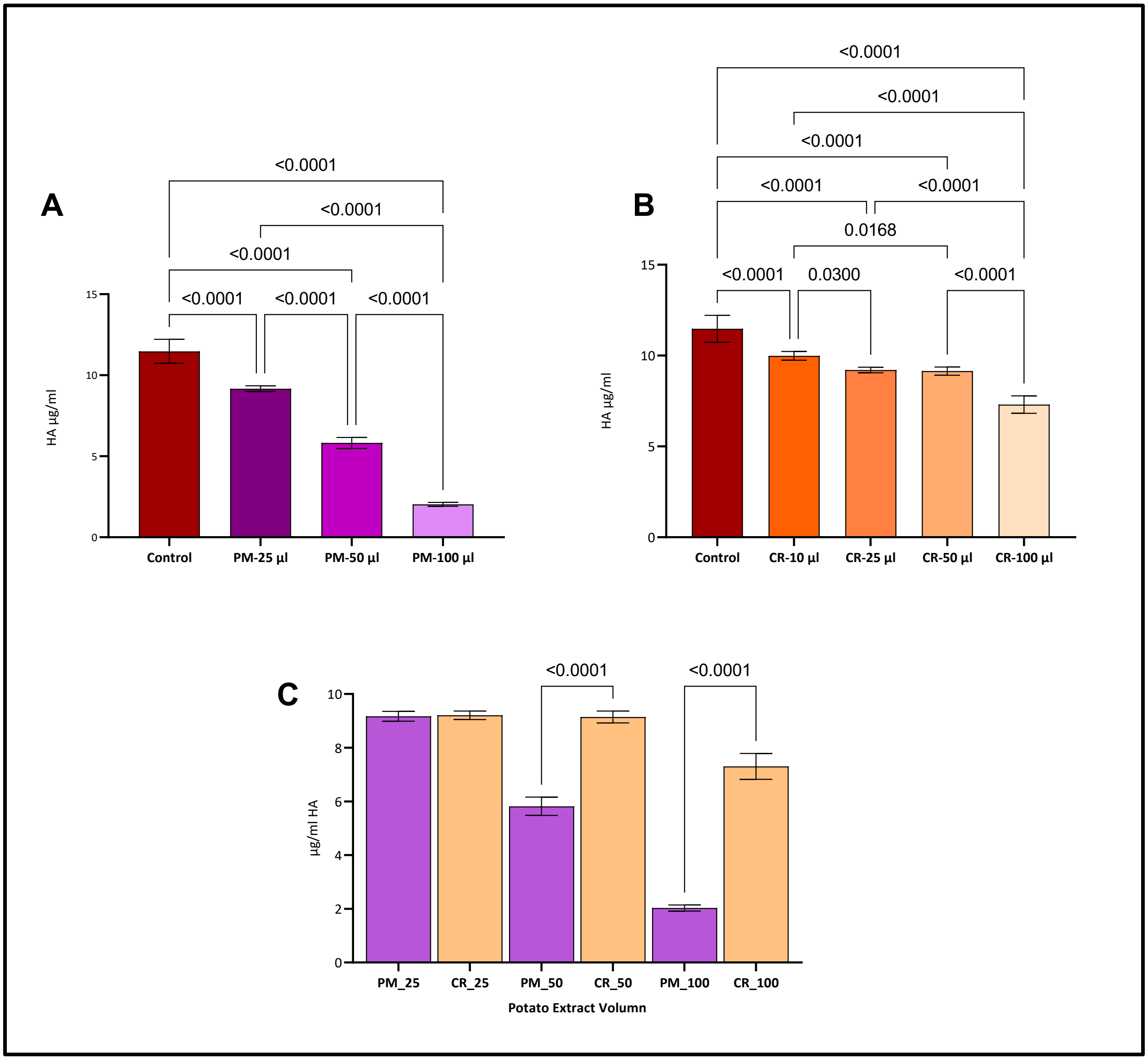


**Figure 2.10.** ACE inhibitory activity of small molecules extracted from cooked potato tubers. A) ACE inhibitory in PM, B) ACE inhibitory in CR. Data represent µg/ml HA production after 30 minutes in presence of different volume/concentration of small molecules. Every 100 µl of PM and CR contained 20 and 13 µg/ml total phenolics, respectively. Data expressed as mean ± SE; n=6/cultivars.

## 2.4. Discussion

The main purpose of this study was to investigate the presence, variation, and bioactivity of phenolic content in different potato genotypes. We utilized in vitro techniques to evaluate the total phenolic content in a population of 57 potato genotypes belonging to five market classes of potato. A targeted analysis of the chlorogenic acid (CGA) composition by HPLC-DAD allowed us to quantify and compare this important phytochemical in 26 genotypes. In another experiment, we evaluated the potential of potato small molecules to inhibit ACE in-vitro.

### 2.4.1. Potato phenolics and relation with antioxidant activity

Potatoes contain numerous phenolic compounds with a wide range of chemical structures, and the composition of these phenolic compounds in potatoes varies among wild or landrace cultivars. As discussed above in section 2.1.4., phenolics are part of the plant defense mechanism which is stimulated in response to pathogens or environmental stress (e.g., UV-B radiations, drought, wounding) (Bennett and Wallsgrove, 1994, Mejdoub-Trabelsi et al., 2020, Akyol et al., 2016). Direct comparison of AOX activity reported in the literature is challenging due to differences in metrology (i.e. units in which the results are reported or the AOX measuring techniques). However, comparison of these methods reveals a trend in the results, which enables the research community to relatively compare these findings. For example, the ORAC (Oxygen Radical Antioxidant Capacity) assay shows a high correlation with total phenolic content assessed by the Folin-Ciocalteu assay (FC) ($R=0.97$, $R^2= 0.75$) (Andre et al., 2009, Lachman et al., 2008). A recent study compared ORAC, cupric ion reducing antioxidant capacity (CUPRAC), trolox equivalent antioxidant capacity (TEAC), ferric reducing antioxidant power (FRAP), and FC methods to measure overall antioxidant in fruit juice (López-Froilán et al., 2018). Their analysis revealed that measurement of total phenolics and the output of the FC test were the most strongly correlated with antioxidant capacity.

In this research we used the FC assay as a high throughput evaluation of the total phenolic content *and* as a measurement of the AOX and reducing capacity of a large population of potato genotypes. Variation in total phenolic content and AOX capacity was observed within and between potato market classes. These genotypes were either released cultivars (e.g., Purple Majesty), or advanced lines (e.g., CO05110_6RU) and all belong to the Colorado State University Potato Breeding and Selection Program. The variation among market class was significant. More specifically, specialty genotypes had a prominent AOX activity and a 112% higher content of total phenolics compared to the Chippers class (Figure 2.1.).

Considerable variation of total phenolic compounds was detected within each market class as well. For example, CO04063_4R/R in the Specialty class had 150% higher total phenolics as compared to CO04067_8R/Y in the same market class. This difference was more prominent in Yellow market class, as we observed a significant difference between the genotypes CO07131_1W/Y and CO00412_5W/Y ($p < 0.005$) with CO07131_1W/Y having 404% higher total phenolics as compared to CO00412_5W/Y (Figure 2.2.).

Our results are aligned with previous research that has shown that the highest phenolic content generally belongs to purple-fleshed tubers. For example, Navarre et. al. reported that microwaved Purple Majesty had 66% higher total phenolics as compared to microwaved Bintje (a white-fleshed genotype) (Navarre et al., 2010). Thompson et al. compared the AOX activity of six cultivars using the ORAC assay and observed that Mountain Rose (a Specialty cultivar) had a significantly higher AOX activity as compared to Purple Majesty (15% higher), and 76% higher when compare to Yukon Gold (Thompson et al., 2009). In our study, using the FC test, we observed that Purple Majesty had a numerically higher phenolic content and AOX capacity in vitro as compared to Mountain Rose (Figure 2.2.), although this difference was not statistically significant. The disparity in results between studies could be the result of using different cultivation years (environment) and different AOX measurements assays (ORAC vs FC). A study investigating 13 Andean genotypes revealed that the Guincho cultivar, with purple skin and flesh, had the highest total phenolics compared to yellow and white flesh cultivars such as Sipancachi and Chata (Andre et al., 2009). Another study investigated the correlation of flesh color and phenolic content in European cultivars. (Lachman et al., 2008). They reported significantly higher total phenolics in purple-fleshed potatoes as compared to yellow cultivars. Specifically, the purple-fleshed genotypes had 54% higher compared to yellow-fleshed genotypes. The same trend was observed in the AOX activity as Valfi and Violette, both purple-fleshed cultivars, had the highest AOX activity (Lachman et al., 2008). Statistically significant variation in one market class, Yellow, has been reported in a total phenol comparison of 4 yellow-fleshed Philippine genotypes. The highest phenolic content and AOX activity were observed in Bengueta when compared to Ganza another yellow flesh cultivar (Rumbaoa et al., 2009). Finally, a broad evaluation of North American potato genotypes demonstrated that genotypes with red and purple skin and flesh color had the highest AOX and total phenolics (e.g., CO112F2–2P/P, CO111F2–1P/P, and ATTX98013–1R/R) (Reddivari et al., 2007a).

### 2.4.2. Potato cultivars' chlorogenic acid content

Overall, our results demonstrate that a high percentage of the total phenolics in potato tubers was represented by CGA, though the percentage of CGA varied among different genotypes (Figure 2.6.). For example, cultivars such as Canela Russet and Russet Burbank had the highest percentage of CGA relative to the total phenolics (34% and 31%, respectively). Interestingly, Canella Russet, is one of the cultivars which has low total phenolics but contained one of the highest percentages of CGA. Other Russets, such as CO07015_4RU and Rio-Grande, also had high ratios of CGA (25% and 24%, respectively). Our results align with previous reports by several groups. One study performed by the potato breeding program in Texas evaluated 8 white and Russet cultivars, named genotypes, and advanced selections, and found that the prominent phenolic was CGA (Blessington et al., 2010). Another study evaluated different market classes, such as Russet, red and purple, and also showed that CGA was the prominent phenolic, with significantly higher concentrations observed in purple and red flesh potatoes (Reddivari et al., 2007b).

2.4.3. The AOX capacity of potato phenolics in vitro is not impacted by cooking.

We observed that cooking potato tubers via microwave did not influence their total phenolic content nor their AOX capacity in vitro. This result is supported by multiple previous studies. For example, microwaving was demonstrated to have the least effect on total phenolics, compared to boiling or frying, as boiling caused phenolics to be leached into the cooking water, which is typically discarded (Blessington et al., 2010, Im et al., 2008, Chuah et al., 2008). Another study determined that antioxidant and total phenolic content of tubers were largely retained by variety of cooking methods (microwaving, steaming, boiling, or baking), though the temperature and timing were the major factors (Navarre et al., 2010). Tsang et al, reported that total phenolics were reduced after boiling and that this was dependent the phenolic structure. For example, they reported that AOX activity of cooked purple majesty was significantly lower compared to raw tubers (a 34% reduction after cooking). The change in specific phenolic compounds were measured by LC-MS and showed that petanin (an anthocyanin compound) was reduced by 83%, while CGA was less affected by cooking (reduced by 10%) (Tsang et al., 2018).

While not addressed in our study, others have demonstrated that the growing environment can impact phenolic quantity but not phenolic composition. Lower minimum daily temperatures during the vegetative period resulted in higher total phenolics and AOX capacity (Lachman et al., 2008). Andre et al., evaluated 13 Andean native potato genotypes in two environments and reported the effects of both factors in the total phenolic content. They showed even though the environmental conditions can significantly affect the total phenolic content, it does not affect the phenolic profile (Andre et al., 2009). Other studies have demonstrated that storage time can affect tuber nutritional quality (e.g., reduction in vitamin C and accumulation of fructose). No significant changes were observed in the phenolic and chlorogenic acid content of the tubers (Goyer et al., 2019). Reddivari and colleagues reported that environment did not impact the concentration of gallic acid or caffeic acid, but did significantly affect CGA (Reddivari et al., 2007b).

### 2.4.4. In vitro ACE inhibition activity of small molecule potato extracts is correlated with total phenolic content.

Another important bioactivity we evaluated was the in vitro ACE inhibitory activity of small molecule extracts of cooked potato tubers. Utilizing our optimized assay, we showed that small molecule extracts from cooked potato tubers can inhibit ACE in vitro and that this activity correlated with total phenolic content of the extracts. For this evaluation, two cultivars were chosen based on our measurement of total phenolic content for 60 potato cultivars. Specifically, we chose a representative low phenolic cultivar (Canela Russet) and high phenolic cultivar (Purple Majesty). While ACE inhibitory activity was observed in both cultivars, the magnitude of ACE inhibition was 2-fold greater in the high phenolic cultivar (Purple Majesty). These results are aligned with previous reports on ACE inhibitory activity of phenolics extracted from different food sources. Phenolic compounds have a demonstrated a role in the reduction of blood pressure through AOX activity and improvement in systemic inflammation, as well as a reduction in RAAS signaling molecules. Phenolic compounds, either as extract from plant material or pure chemicals, have been shown to significantly reduce blood pressure in the hypertensive rat (Agunloye and Oboh, 2018, Kozuma et al., 2005). One of the mechanisms by which phenolics reduce blood pressure is their ACE inhibitory activity. Pre-clinical research has revealed that oral gavage of these phenolic compounds significantly lowers ACE activity in plasma in a dose-dependent manner. Ex-vivo studies have shown that phenolic compounds can be released after in vitro digestion and accumulatively exert ACE inhibitory activity (Zieliński et al., 2020, Kozuma et al., 2005, Dalar and Konczak, 2014).

Most of these studies have focused on evaluating the presence of inhibitory activity of an extract from one plant cultivar/species. There are limited explorations of the effect of various phenolic content in food or extracts. Abdullah et al., evaluated fourteen species of culinary-medicinal mushrooms for their antioxidant activity and ACE inhibitory in-vitro (Abdullah et al., 2012). They reported that the most potent species for ACE inhibition also had the highest AOX activity. Recently, a group in Spain explored the variation among different winery byproducts for their phenolic content and ACE inhibitory activity. They observed that ACE inhibitory activity and phenolic profiles varied among different byproducts which also showed different intensity in reducing blood pressure in hypotensive rat (López-Fernández-Sobrino et al., 2021).

There is a limitation in our understanding of the potential for commodity crops such as potato to inhibit ACE activity. To our knowledge, this is the first report of ACE inhibitory activity of small molecule extracts from potato and the first to demonstrate that this activity varies among different cultivars. Importantly, our results demonstrate that genotype and flesh color can be an indicator of ACE inhibitory potential in vitro. Coupled with other reports of ACE inhibitory activity of potato protein hydrolysate (Pihlanto et al., 2008), these results support the potential of potato as a health promoting commodity crop. Additional research is needed to investigate the effect of potato as a whole food on ACE activity.

Taken together, the results of this study provide an important first step in the evaluation of potato for human health.  This information can be leveraged by both consumers (e.g., industry) and breeders. Through the thousand years of conventional or modern breeding the focus has been to increase the tuber size and calorie content and reduce toxic alkaloids. Many nutritious phytochemicals have been lost during these selections, as they are not very concentrated? in popular big tuber cultivars. With the emphasis on improving the nutritional value of crops beyond their calorie content, more attention is being paid to enhancing phytochemical content. The vast biodiversity of potato, with over 5,000 cultivars, provides the opportunity to investigate the presence and activity of these phytochemicals, even in landrace and wild species. Also, survival of a substantial amount of potato phenolics during microwaving signify that breeding for higher phenolic cultivar to improve food AOX is a logical approach.

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CHAPTER 3:

# A NON-TARGETED METABOLOMICS APPROACH TO EVALUATE THE EFFECT OF HIGH PHENOLICS POTATO ON OBESE AND LEAN ANIMAL MODELS

## 3.1. Introduction

### 3.1.1 Obesity, the driver of cardiometabolic disease

Today, there is growing evidence showing that changes in diet can improve or prevent life-threatening cardiometabolic disease (CMD) risk, resulting in a trend of making healthy eating a priority for consumers. Obesity is considered a primary risk factor for the development of CMD, the prevalence for which continues to rise worldwide. Current estimates show that roughly 3 in 4 Americans are considered overweight or obese (CDC and NCHS, 2021, CDC, 2018). A sedentary lifestyle, poor dietary patterns (e.g., 'Western-type' diet, high in saturated fat, sugar, and refined grain), and other environmental factors (e.g., socioeconomic status) have created an 'obesogenic environment' that continues to fuel the obesity pandemic. Diseases associated with obesity, like CMD, are driven largely by deleterious adaptations which occur broadly throughout the body, such as immune dysfunction, gut dysbiosis, dyslipidemia, and insulin resistance (Nagpal et al., 2018, Frydrych et al., 2018, Cao, 2014, Shen et al., 2013).

### 3.1.2. Obesity and systemic chronic inflammation, linkage to CMD

It is now understood that systemic chronic inflammation is the key underlying factor in the pathophysiology of obesity and obesity-associated diseases, such as CMD (Bastard et al., 2000, Mehta et al., 2010, Phosat et al., 2017, Uemura et al., 2017, Virdis et al., 2018). Obesity is characterized by the excessive accumulation of weight as adipose tissue. Found throughout the body, adipose tissue is heterogeneous with some depots displaying different inflammatory phenotypes than others. For example, visceral adipose tissue, which makes up the intra-abdominal fat surrounding organs, is considered to be more pro-inflammatory than subcutaneous adipose tissue and is associated with disease risk. Inflammation is a protective response, normally involving the acute upregulation of inflammatory activities which resolve once the threat has been removed. However, certain lifestyle risk factors, such as obesity, are known to inhibit the resolution of acute inflammation, and in turn, promote the development of systemic chronic inflammation. Shifts in the inflammatory response from acute to chronic lead to a breakdown in immune tolerance, causing cell and tissue level damage, as well as impairing normal immune function. Circulating inflammatory cytokines such as C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor (TNF), and monocyte chemoattractant protein-1 (MCP-1) are elevated in obese individuals compared to lean counterparts (Ghanim et al., 2004, Ghanim et al., 2009, Virdis et al., 2018). More so, higher levels of circulating inflammatory cytokines are associated with obesity, CVD (Low Wang Cecilia et al., 2016, Ridker et al., 2000) insulin resistance, and T2D (Ridker et al., 2000, Shoelson et al., 2006). Multiple pathways have been proposed to incite the development of inflammation associated with obesity - most of which stem from gastrointestinal (GI) tract dysfunction such as a high-fat diet, gut dysbiosis, and intestinal barrier dysfunction 'leaky gut'. Although multifaceted, leaky gut has emerged as a significant contributor to the development of obesity-associated inflammation.

### 3.1.3. Potatoes can provide a healthy diet

Many dietary approaches for weight control are currently available to the public, and each purport to offer advantages for the prevention of disease risk such as CMD. However, the rigidity of these diets, which do not permit access to foods individuals enjoy, makes sustaining them a challenge. In general, a sustainable and healthy diet can be described as affordable, environmentally sustainable, culturally acceptable, accessible, and nutritionally adequate food

(FAO, 2012, Van Loo et al., 2017). Potatoes offer a low carbon footprint and high-quality nutrients at an affordable price (USDA/ERS, 2019, Xu et al., 2020).

Potato compounds either as an extract supplemented into the diet or as a part of the whole food matrix, show satiating properties. In addition to the effects of potato protein and PI extracts, consumption of isoenergetic portions of whole potatoes, particularly boiled, appear to be more satiating compared to other starchy carbohydrates like white and brown rice, and white beans (Geliebter et al., 2013, Lee et al., 2019, Johnston et al., 2020). When ad libitum consumption is permitted, about 40% less energy is consumed in mixed meals containing potato, compared to rice and pasta (Erdmann et al., 2007, Akilen et al., 2016).

Nevertheless, in all these studies only white-fleshed potatoes has been evaluated. The myriad of other available potato cultivars which contain variation in phenolics and other macro- and micronutrients presents a tremendous opportunity for the development of nutritional foods to combat obesity.

#### 3.1.4. High phenolic potato as a path to improve cardiometabolic health

Phenolics have drawn much attention as functional phytochemicals against obesity and obesity-induced biochemical changes in human and rodent studies (Rock et al., 2008, Mastroiacovo et al., 2014, Lockyer et al., 2017). Specifically, supplementing a high fat diet with phenolic extracts from different plant sources has been shown to greatly reduce body weight, visceral fat mass, serum leptin and insulin levels, and triglyceride and cholesterol content within the liver and adipose tissue of rodents (Cho et al., 2010, Bhandarkar et al., 2019, Huang et al., 2015b). Studies attribute some of the beneficial effects mediated by phenolics to an increase in satiety and a reduction in lipase and amylase activity (Molan et al., 2008, Ríos-Hoyo and Gutiérrez-

Salmeán, 2016, Bajerska et al., 2016, Coe and Ryan, 2016, Castro-Barquero et al., 2018, Xu et al., 2019).

Potatoes with a higher phenolic concentration have shown promise for alleviation of risk factors associated with CMD. Specifically, daily intake of the phenolic-rich potato (Purple Majesty) led to improvements in pulse wave velocity and arterial blood pressure within healthy adults (SBP and DBP) (Vinson et al., 2012, Tsang et al., 2018). Additional studies report an improvement in glucose and lipid profile, oxidative stress, and inflammatory biomarkers within the serum of subjects fed a high-phenolic potato compared to controls fed a low-phenolic potato (Kaspar et al., 2011, Han et al., 2007, Choi et al., 2013, Kubow et al., 2014).

Prebiotics in potatoes, such as potato resistant starches (RS), are another newly emerging factor shown to be important within the diet. Recent clinical and preclinical studies demonstrate that RS enhanced satiety, reduced weight gain, improved blood lipids and glucose levels, and increased favorable gut bacteria in the colon, responsible for producing SCFAs (Han et al., 2008). Although these compounds have been detected and profiled among potato genotypes, their biological effects on the metabolism have not yet been addressed.

Investigations on the health impact of potatoes have traditionally focused on individual constituents, such as proteins, fats, carbohydrates, and micronutrients, despite the fact that our diets are multifaceted and do not consist of one single molecule. Rather, food products, which coalesce to form our unique dietary habits, are complex matrices of bioactive compounds and form intricate networks which ultimately influence the bioavailability and bioactivity of each other. For example, we know that macronutrients, like proteins, carbohydrates, and lipids can surround small molecules, more specifically phenolics, and modulate their bioavailability and absorption (Ortega et al., 2009, Saura-Calixto, 2011, Han et al., 2019). On the other hand, phenolics are known to affect the bioavailability of macromolecules by regulating carbohydrate metabolism and decreasing the glycemic response, as well as modulating lipid and protein absorption and metabolism (Gorelik et al., 2005, Gorelik et al., 2013, Chai et al., 2013). Contradictory effects have also been reported between protein and phenolics regarding their effect on each other's bioavailability, ranging from negative to neutral and positive (Helal et al., 2014). Altogether this highlights the complexity of food matrices and the reciprocal regulation that exists among nutrients. As such, the traditional view on food recommendations, which has been based solely on carbohydrate, protein, and fat content, is being modified to incorporate the evaluation of food as a complex chemical matrix. Although many studies report a close association between the compositional pattern of food and health, there is still insufficient evidence allowing us to discern how these other players might interact with the satiating effects of potatoes. More so, it remains unclear as to whether phytochemicals within potato genotypes can enhance the health benefits of this crop in terms of modulating pathways involved in obesity and inflammation. Thus, to more accurately evaluate the potential of potatoes as a healthy diet strategy we need to 1) consider the variation of these bioactive compounds in different potato cultivars, and 2) study the interaction of these bioactive compounds with other compounds and how this modulates health outcomes. Considering there is no single player responsible for energy regulation and body weight outcomes, I hypothesize that bioactive compounds consumed as part of a diet containing a high phenolic potato cultivar will affect various pathways involved in energy hemostasis and inflammation resulting in improved health outcomes compared to a non-potato diet control.

## 3.2. Experimental Procedure

### 3.2.1. Production and preparation of experimental diets

Potato tubers (Purple Majesty) were provided by Colorado State University Potato Breeding and Selection Program. Tubers were washed under tap water to make sure there was no soil residue left on the skin, then rinsed under distilled water. The tubers were cooked using a method previously developed in or laboratory by Chapparo et al., (Chaparro et al., 2018). Briefly, the fresh weight of each potato was used to calculate the cooking time, where 30 g of potato fresh weight was cooked (microwaved) for 1.75 min at 400 W power. After cooking, potato tubers were immediately frozen in liquid nitrogen and kept at -80 C. Cooked frozen tubers were shattered using a hammer and freeze-dried. The freeze-dried samples were ground into powder using a coffee grinder (Krups, krupsusa.com). The fine powders were used in preparation of the rodent pellet diet (NEVIGO, Madison, WI).

The two diets (control and potato diet) were isocaloric. The control diet (control) was designed based on the AIN-93M diet and was formulated to contain approximately 24.4% amylose, 16.3% amylopectin, and 15% sucrose. The starch source in the AIN-93M diet was cornstarch (containing 22.5% amylose and 67.5% amylopectin). The purple potato (potato) diet contained a 50% purple potato flour diet based on AIN-93M, which the source of starch switched to potato starch (48.8% amylose and 32.5% amylopectin).

### 3.2.2. Animals and experimental design

Male (2 months old) leptin-deficient mice homozygous for the obese spontaneous mutation Lepob (ob/ob) (we refer to as obese) and heterozygous (+/ob) controls (we refer to as lean) were obtained from Jackson Laboratory. Mice were individually housed in a temperature (25°C) and humidity-controlled (50-60%) environment on a 12h:12h light-dark cycle. Mice were acclimatized to the housing conditions for 2 weeks prior to initiating experimental procedures. All animal procedures were reviewed and approved by the Colorado State University Institutional Animal Care and Use Committee. Mice received either a purple potato diet (potato, n=20) (TD.180814) or HAMS control diet (control, n=20) (TD.180813) for 9 weeks. Mice were allowed ad libitum access to food and water for the duration of the studies. Bodyweight and food intake were measured weekly.

### 3.2.3. Food uptake and adiposity measurement

Mouse body weight and their food intake were monitored daily for 11 weeks. Food pellet was provided daily to enable measurement of intake from day before. The adipose tissues were collected at the end of study. The tissues were weighted separately and placed in bag and directly submerged in liquid nitrogen. The tissue kept at -80C until the day of processing.

### 3.2.4. Sample processing for metabolomics analysis

Samples (serum and liver tissue) were collected from animals (both genotypes: obese and lean) who have been fed the 2 different diets (n=10 mice/diet). The liver samples were flash frozen in the liquid nitrogen after the excision and transferred to -80 °C till further analysis. Then all samples were freeze-dried, and the powder was stored at -80 C till the extraction. The powder was then weighed (25 mg) and homogenized in cold MTBE (1 ml). After vortexing, sample were sonicated for 1 hour in cold water (4 °C), followed by addition of the same volume of HPLC grade water (1 ml), and vortexing for another 30 minutes. The organic and aqueous layers were separated by centrifugation (15 minutes at 3500 rpm), transferred to new tubes and dried separately under a nitrogen dryer. The organic layer was resuspended in toluene: methanol (1:1 v/v) for analysis by liquid chromatography–mass spectrometry (LC–MS). The aqueous layer was resuspended in acetonitrile/methanol/water (2:2:1) and then derivatized by trimethylsilyl/methoximation as described in (Broeckling et al., 2014, Yao et al., 2019) for gas chromatography–mass spectrometry (LC–MS) analysis. Briefly, 50 µl of the aqueous phase was dried under nitrogen, resuspended in 50 µl of pyridine containing 25 mg/mL of methoxyamine hydrochloride, incubated at 60°C for 45 min, vigorously vortexed for 30 s, sonicated for 10 min, and incubated for an additional 45 min at 60°C. Next, 50 µl of N-methyl-N-trimethylsilyltrifluoroacetamide with 1% trimethylchlorosilane (MSTFA + 1% TMCS, Thermo Scientific) was added and samples were vigorously vortexed for 30 s followed by incubation at 60 °C for 30 min.

Serum samples were stored at -80 C. A portion of the serum was retained for cytokine and immune cell analysis (data described elsewhere), and 100 µl was used for extraction of t metabolites as described above. Briefly, a 100 µl of serum mixed with cold Methyl tertiary-butyl ether (MTBE) (1 ml). After vortexing, sample were sonicated for 1 hour in cold water (4 C), followed by addition of the same volume of HPLC grade water (1 ml) was added, and samples were vortexed for another 30 minutes. Then the organic and aqueous layers were separated by centrifugation (15 minutes at 3500 rpm), pippeted into different tubes and dried separately under a nitrogen dryer. The organic layer was resuspended in toluene: methanol (1:1 v/v) for analysis by LC-MS. The aqueous layer was resuspended in acetonitrile/methanol/water (2:2:1) and is further derivatized by trimethylsilyl/methoximation as described in (Broeckling et al., 2014, Yao et al., 2019) for GC-MS analysis. Briefly, 50 µl of the aqueous phase was dried under nitrogen, resuspended in 50 µl of pyridine containing 25 mg/mL of methoxyamine hydrochloride, incubated at 60 °C for 45 min, vigorously vortexed for 30 s, sonicated for 10 min, and incubated for an additional 45 min at 60°C. Next, 50 µl of N-methyl-N-trimethylsilyltrifluoroacetamide with 1% trimethylchlorosilane (MSTFA + 1% TMCS, Thermo Scientific) were added, and samples were vigorously vortexed for 30 s, incubated at 60 °C for 30 min.

### 3.2.5. Metabolite Detection Using Ultra Performance Liquid and Gas Chromatography-Mass Spectrometry (LC and GC-MS):

Quality control (QC) samples were prepared to verify the instrument reliability as well as to make sure the analysis by LC-MS and GC-MS was consistent. The QC samples were generated as a pool from each extracted liver or serum sample and were injected after every $6^{th}$ sample. LC-MS and GC-MS samples were injected in randomized order. The organic phase from the extraction was analyzed by LC-MS (positive and negative electrospray ionization modes) and the aqueous phase from the extraction was derivatized (described above) and analyzed by GC–MS.

For the LC-MS analysis, one microliter of the extract was injected into a Waters Acquity UPLC system. Separation was achieved using a Waters Acquity UPLC CSH Phenyl Hexyl column (1.7 µM, 1.0 x 100 mm), using a gradient from solvent A (Water, 2mM ammonium formate with 0.1% formic acid) to solvent B (Acetonitrile, 0.1% formic acid). Injections were started at 99.9% solvent A, held at 99.9% A for 1 min, ramped to 95% B over 12 minutes, held at 95% B for 3 minutes, returned to starting conditions over 0.05 minutes, and allowed to re-equilibrate for 3.95 minutes, with a 200 µL/min constant flow rate. The column and samples were held at 65 °C and 6 °C, respectively. The column eluent was infused into a Waters Xevo G2 Q-TOF-MS with an electrospray source in both positive and negative mode, scanning 50-2000 m/z at 0.2 seconds per scan, and alternating between MS (6 V collision energy) and MSE mode (15-30 V ramp). Calibration was performed using sodium iodide with 1 ppm mass accuracy. The capillary voltage was held at 2,200 V, source temperature at 150 °C, and nitrogen desolvation temperature at 300 °C (350 °C for negative mode) with a flow rate of 800 and 600 L/hr for positive and negative mode, respectively.

For GC-MS analysis, metabolites were detected using a Trace 1310 GC coupled to a Thermo ISQ mass spectrometer. Samples (1 µL) were injected at a 10:1 split ratio to a 30 m TG-5MS column (Thermo Scientific, 0.25 mm i.d., 0.25 µm film thickness) with a 1.2 mL/min helium gas flow rate. GC inlet was held at 285 °C. The oven program started at 80 °C for 30 s, followed by a ramp of 15 °C/min to 330 °C, and an 8 min hold. Masses between 50-650 m/z were scanned at 5 scans/sec under electron impact ionization. Transfer line and ion source were held at 300 and 260 °C, respectively.

### 3.2.6. Metabolomics data processing

Data was processed as previously described by Broeckling and colleagues (Broeckling et al., 2014, Broeckling et al., 2013, Yao et al., 2019). Briefly, for each sample, raw data files were converted to .cdf format and a matrix of molecular features as defined by retention time and mass (m/z) was generated using XCMS software in R for feature detection and alignment. Features were grouped using RAMClustR with TIC normalization. LC-MS data were first annotated by searching against an in-house spectrum and retention time database using RAMSearch. RAMClustR was used to call the findMain function from the interpret MSSpectrum function (MS-FINDER program v2.40 (Tsugawa et al., 2016, Lai et al., 2018) to infer the molecular weight of each LC-MS compound for annotation of the mass signals. The complete MS spectrum and a truncated MSE spectrum were written to a .mat format for import to MSFinder. The MSE spectrum was truncated to include only masses with values less than the inferred M plus its isotopes, and the .mat file precursor ion was set to the M+H ion for the findMain inferred M value. These .mat spectra were analyzed to determine the most probable molecular formula and structure. MSFinder was also used to perform a spectral search against the FooDB, HMDB, ChEBI, and Lipidmaps metabolite databases (foodb.ca; hmdb.ca; ebi.ac.uk/chebi; lipidmaps.org). All results were imported into R and a collective annotation was derived with prioritization of MSFinder mssearch > MSFinder structure > MSFinder formula > findMain M. All R work was performed using R version 3.3.1. GC–MS data were annotated using spectral and retention index matching within AMDIS software using the Golm Metabolome Database (Kopka et al., 2005).

### 3.3. Data analysis

Statistical analyses were performed with R (R Foundation for Statistical Computing, Vienna, Austria), GraphPad Prism version 9 (GraphPad Software, USA, California) and SIMCA (SIMCA 17, Sartorius, Goettingen, Germany). Data were Z-score transformed and UV scaled prior to multivariate statistical analysis. A one-way ANOVA with Tukey's post hoc test was used to determine significance between different genotypes and diets and for all other comparisons. Univariate statistical results for metabolite data were adjusted for multiple testing using the Benjamini-Hochberg procedure. Significance was based on an adjusted *P-value* $< 0.05$.

## 3.4. Results:

### 3.4.1. Potato diet reduce food intake and adiposity in obese and lean animals.

At the study outset, there was no statistical difference in body weight within each genotype group (obese and lean). At the end of the study, animals in the obese group on the control diet had significantly greater body weight than animals on the potato diet (*P* < 0.001 (Table 3.1., Figure 3.1. A).

**Table 3.1.** Animal weekly body weight during feeding treatment.

| Means | Obese-Control (g) | Obese-Potato (g) | Lean-Control (g) | Lean-Potato (g) |
|---|---|---|---|---|
| week 1 | 46.3 ± 5.7 | 46.3 ± 5.7 | 27.2 ± 1.8 | 27.7 ± 1.9 |
| week 2 | 45.2 ± 5.7 | 45.2 ± 5.7 | 27.4 ± 1.8 | 27.6 ± 2.0 |
| week 3 | 44.9 ± 5.9 | 44.9 ± 5.9 | 28.0 ± 2.1 | 28.0 ± 2.1 |
| week 4 | 44.8 ± 5.8 | 44.8 ± 5.8 | 28.5 ± 2.1 | 28.2 ± 1.8 |
| week 5 | 45.4 ± 5.6 | 45.4 ± 5.6 | 29.5 ± 2.1 | 28.7 ± 1.5 |
| week 6 | 46.6 ± 4.8 | 46.5 ± 4.8 | 30.1 ± 2.0 | 28.8 ± 1.4 |
| week 7 | 46.7 ± 4.3 | 46.7 ± 4.3 | 30.6 ± 1.9 | 28.8 ± 1.7 |
| week 8 | 47.3 ± 4.1 | 47.3 ± 4.1 | 30.7 ± 1.9 | 29.0 ± 1.8 |
| week 9 | 46.8 ± 4.2 | 46.8 ± 4.2 | 30.8 ± 1.9 | 29.2 ± 2.3 |
| week 10 | 47.9 ± 4.2 | 47.9 ± 4.2 | 31.3 ± 2.0 | 29.8 ± 1.8 |
| Week 11 | 47.6 ± 4.6 | 47.649 ± 4.6 | 31.3 ± 1.5 | 29.8 ± 1.6 |

Data expressed as mean ± SE; n=9-10 mice/group.

During the 9 weeks animals were exposed to the diet treatment, both the obese and lean groups on the control diet were observed to have significantly higher food intake as compared to animals on the potato diet (P < 0.001 and P = 0.009, respectively; Table 3.2., Figure 3.1. A). While not significant, a similar trend was observed in the lean animals (Table 3.2., Figure 3.1. A).

**Table 3.2.** Animal weekly food intake during feeding treatment.

| Means | Obese Control (g/day) | Obese Potato (g/day) | Lean Control (g/day) | Lean Potato (g/day) |
|---|---|---|---|---|
| week 1 | 3.9 ± 0.6 | 3.0 ± 0.5 | 3.3 ± 0.5 | 2.94 ± 0.3 |
| week 2 | 3.9 ± 0.7 | 3.3 ± 1.1 | 3.6 ± 0.3 | 3.41 ± 0.3 |
| week 3 | 4.4 ± 0.5 | 3.2 ± 0.5 | 3.8 ± 0.3 | 3.44 ± 0.4 |
| week 4 | 3.6 ± 0.4 | 3.0 ± 0.3 | 3.3 ± 0.28 | 3.19 ± 0.5 |
| week 5 | 4.2 ± 0.4 | 3.3 ± 0.3 | 3.5 ± 0.3 | 3.1 ± 0.4 |
| week 6 | 4.0 ± 0.4 | 3.1 ± 0.3 | 3.4 ± 0.33 | 3.0 ± 0.2 |
| week 7 | 3.9 ± 0.3 | 3.0 ± 0.2 | 3.5 ± 0.34 | 3.0 ± 0.2 |
| week 8 | 3.9 ± 0.3 | 3.2 ± 0.24 | 3.4 ± 0.3 | 3.2 ± 0.4 |
| week 9 | 3.7 ± 0.4 | 2.9 ± 0.3 | 3.3 ± 0.4 | 3.0 ± 0.3 |
| week 10 | 3.7 ± 0.3 | 3.0 ± 0.2 | 3.3 ± 0.35 | 2.9 ± 0.2 |
| Week 11 | 3.6 ± 0.3 | 2.9 ± 0.2 | 3.4 ± 0.38 | 3.1 ± 0.2 |
| Average | 3.89 ± 0.08 | 3.08 ± 0.05 | 3.45 ± 0.05 | 3.1 ± 0.05 |

Data expressed as mean ± SE; n=9-10 mice/group.

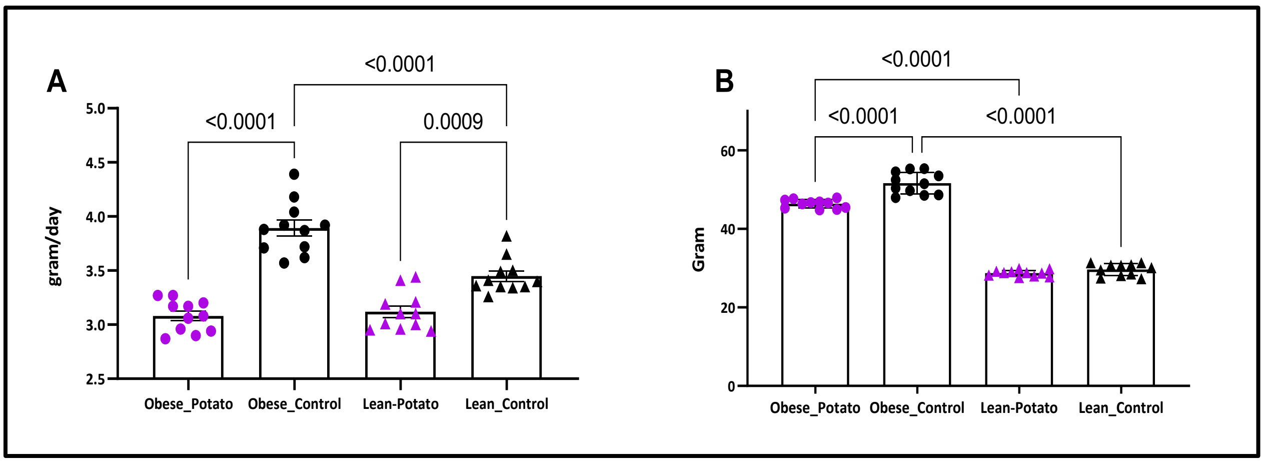


**Figure 3.1:** Change in food intake (A) and body weight (B) among two genotypes and two diet groups, after nine weeks on either Purple Majesty Potato Diet (potato) or control (Control) diet. Statistical analysis was performed using two-way ANOVA with Tukey's post hoc test. Data expressed as mean ± SE; n=9-10/group.

Measurement of visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and perivascular adipose tissue (PAT) were taken at the study end point. Interestingly, we observed a significant ($P < .001$) reduction in adiposity (SAT, VAT and PAT) in lean animals (Figure 3.2, A, C and E) on the potato diet compared to the control, even though the overall weight reduction of this group was not significant (Figure 3.1. B). We also observed a significant decrease in subcutaneous and visceral adiposity in obese animals on the potato diet as compared to controls ($P = .02$ and $P < .01$ respectively) diet (Figure 3.2, A and B).

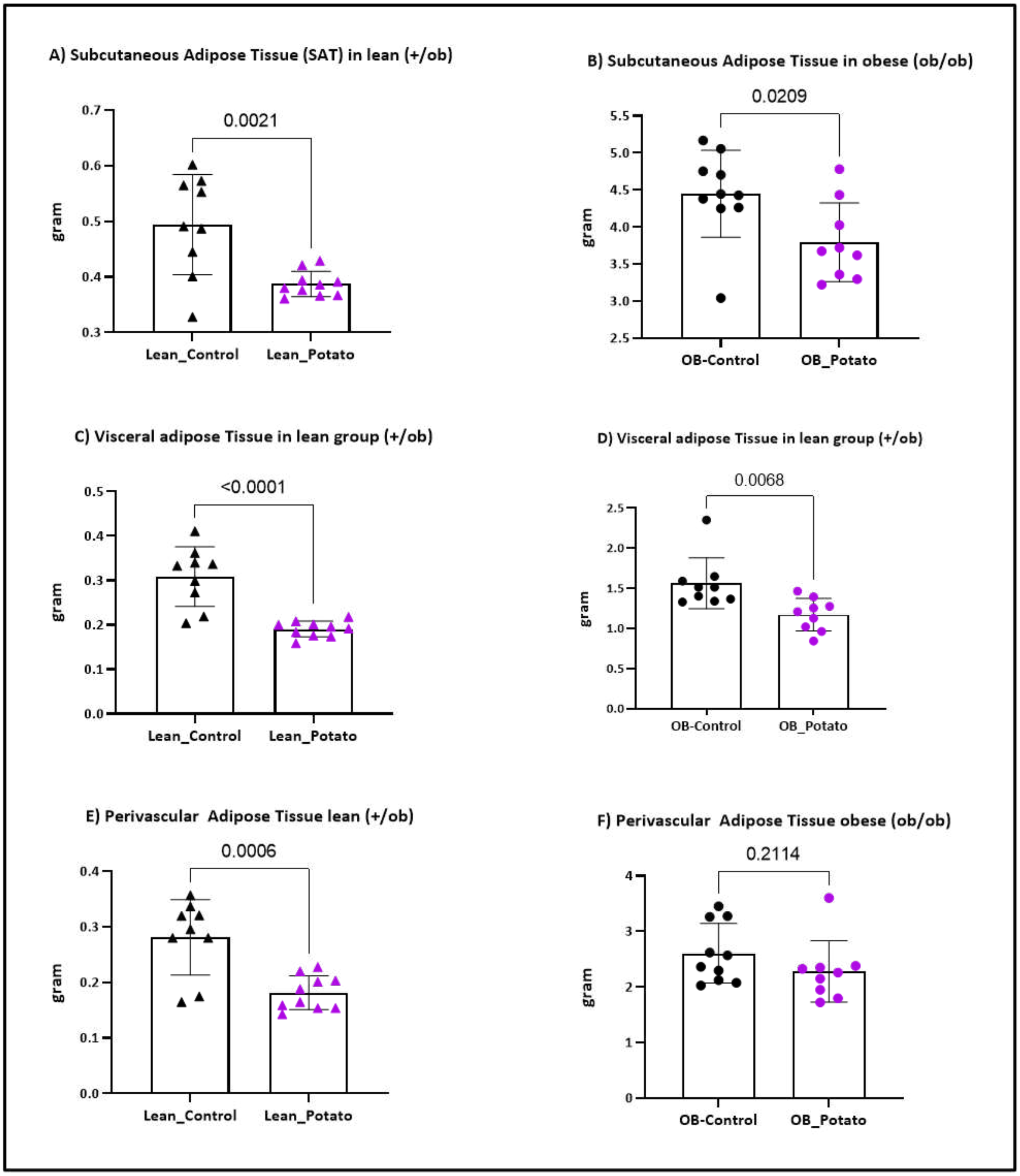


**Figure 3.2:** Adipose tissue weight, measured after nine weeks of potato or control diet. (A) Subcutaneous adipose tissue in lean group (A) and obese (B) Visceral adipose tissue in lean group (C) and obese (D) Perivascular adipose tissue in lean group (E) and obese (F) Statistical analysis was performed using one-way ANOVA with Tukey's post hoc test. Data expressed as mean ± SE; n=9-10/group.

3.4.2. Metabolite variation was observed among lean and obese animals, regardless of diet.

A total of 1274 and 417 metabolites were annotated in liver and serum samples, respectively. Clear shifts in the metabolite profile from both serum and liver were observed in the obese animals (including animals from both the potato and control diet) as compared to the lean animals (Figure 3.3.).

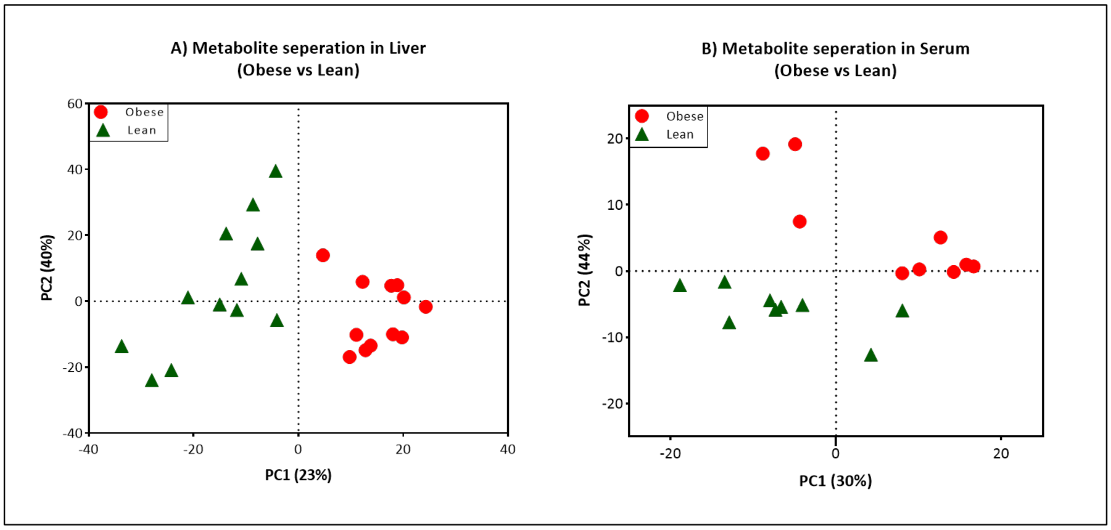


**Figure 3.3.** Principal components analysis (PCA) scores plots of metabolites from obese vs lean animals inclusive of both control and potato diet in A) liver and B) serum. Percent variation explained by each principal component is indicated for PCA has been performed on 1274 and 417 metabolites in the liver and serum respectively. A) liver PC1 and PC2 scores plot, and B) serum PC1 and PC2 scores plot.

A volcano plot was used to visualize the metabolites with a fold change of 2 and higher, and adjusted $P < 0.05$ in the liver of obese and lean animals (Fig 3.4. C). Under these criteria, 29 metabolites were significantly higher in obese animals and 22 metabolites were significantly higher in lean animals. Figure 3.4. A and B shows the chemical class of all the metabolites that are significantly higher in the serum of obese (B) and lean (A) animals (adjusted P-value < 0.05, no fold change filter).

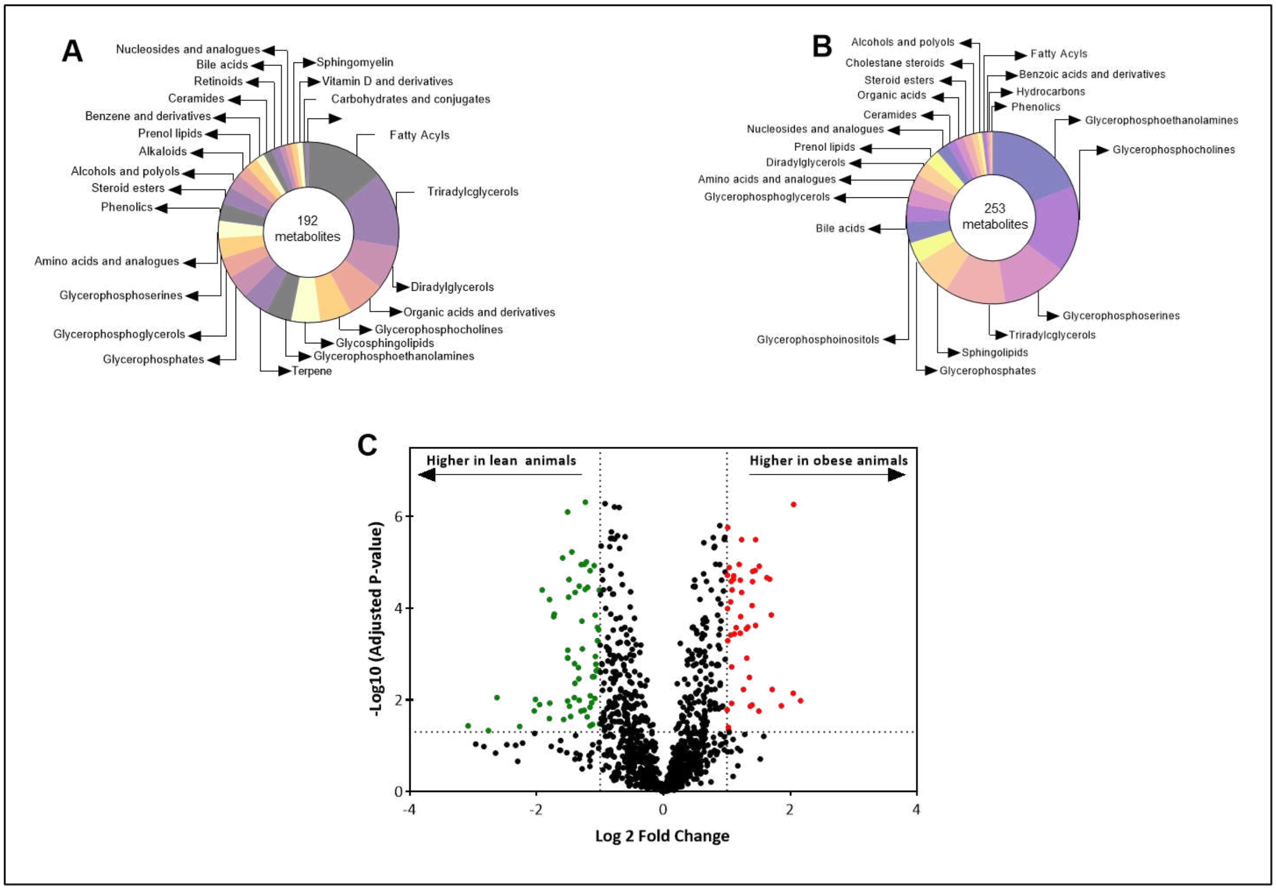


**Figure 3.4.** Metabolite variation in the liver of obese and lean animals. Volcano plots comparison between the lean and obese animals in the liver (C). Red points represent metabolites that are higher in obese animals (fold change ≥ 2; adjusted $P \leq 0.05$). Green points represent the metabolites that are higher in lean animals (fold change ≥ 2; adjusted $P \leq 0.05$). Portion plots (A and B) represent the chemical class of all metabolites that were significantly higher (adjusted $P \leq 0.05$, no fold change filter) in lean (A) and obese (B) animals.

Among the compounds that are driving this separation in the liver (between obese and lean animals), glycero-phospho-ethanol-amines, triglycerides, and glycerophosphocholines were a prominent group that were higher in abundance in obese animals (Fig 3.4. B). Bile acids, cholesterol esters and ceramides, were also higher in abundance in the obese group.

Serum metabolites also shows separation in PCA analysis (Fig 3.3. B), and a volcano plot was again used to visualize the metabolites with fold change of 2 and higher, and adjusted $P <$

0.05 (Fig 3.5. C). Under these criteria, 10 metabolites were significantly higher in abundance in obese animals and only one metabolite was significantly higher in abundance in lean animals. Figure 3.5. A and B shows the chemical class of all the metabolites that are significantly higher (adjusted P-value < 0.05 no fold change filter) in the serum of obese (B) and lean (A) animal.

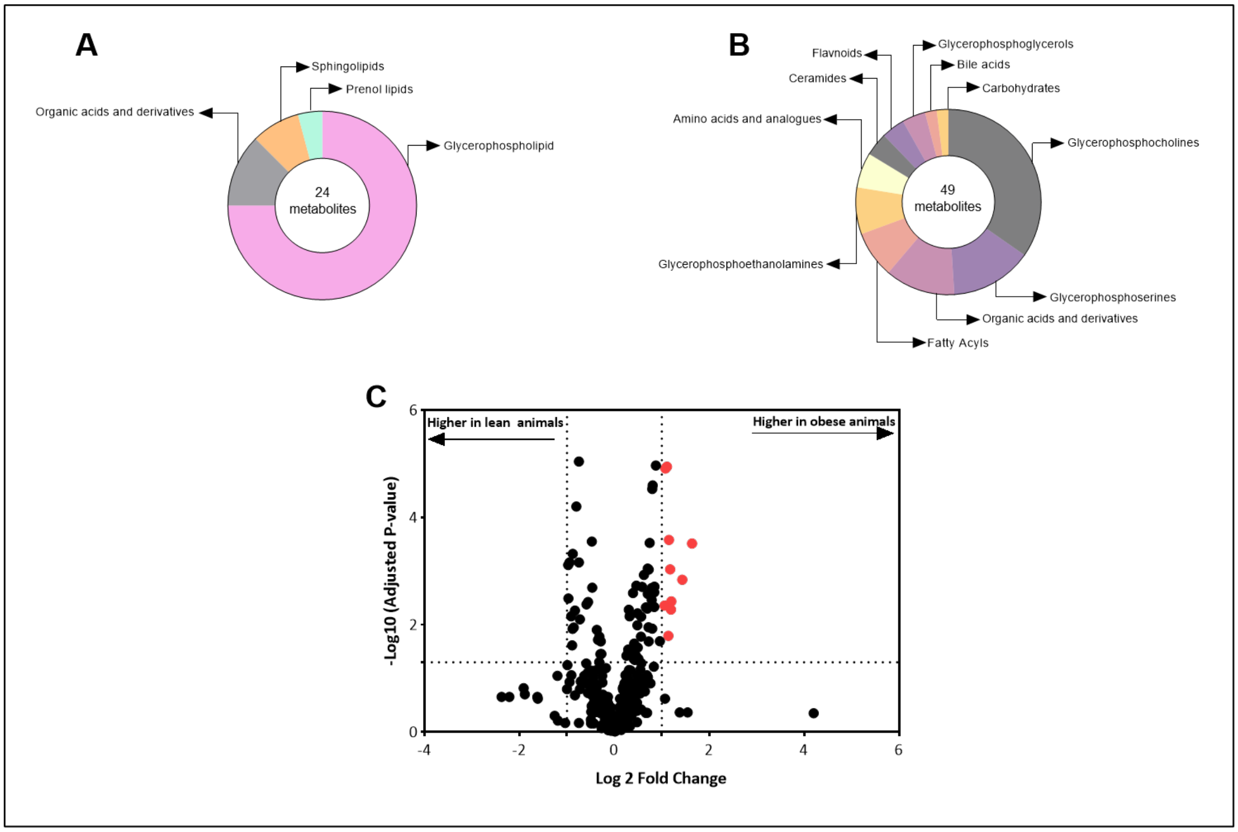


**Figure 3.5.** Metabolite variation in serum of obese and lean animals. Volcano plots comparison between the lean and obese animals in the serum (C). Red points represent metabolites that are higher in obese animals (fold change ≥ 2; adjusted P ≤ 0.05). Green points represent the metabolites that are higher in lean animals (fold change ≥ 2; adjusted *P* ≤ 0.05). Portion plots (A and B) represent the chemical class of all metabolites that were significantly higher (adjusted *P* ≤ 0.05, no fold change filter) in the serum of lean (A) and obese (B) animals.

### 3.4.3. The potato diet influenced metabolism

Our results also demonstrate that the overall metabolite profile in the liver and serum is affected by the potato diet. Animals on the potato diet, in either obese or lean group, separated by PCA (Fig 3.6. and 3.7.). As shown in Figure 3.6. the liver metabolites from obese animals (Fig 3.6.A) separate primarily along PC3 (56%), whereas the serum metabolites from obese animals separate more prominently on PC 2 (57%) (Fig 3.6. C). Eight liver metabolites were significantly higher in abundance (adjusted $P$-value < 0.05, fold-change < 2) in animals on the potato diet compared to the control diet (Fig 3.6. B). No serum metabolites were significant using these criteria.

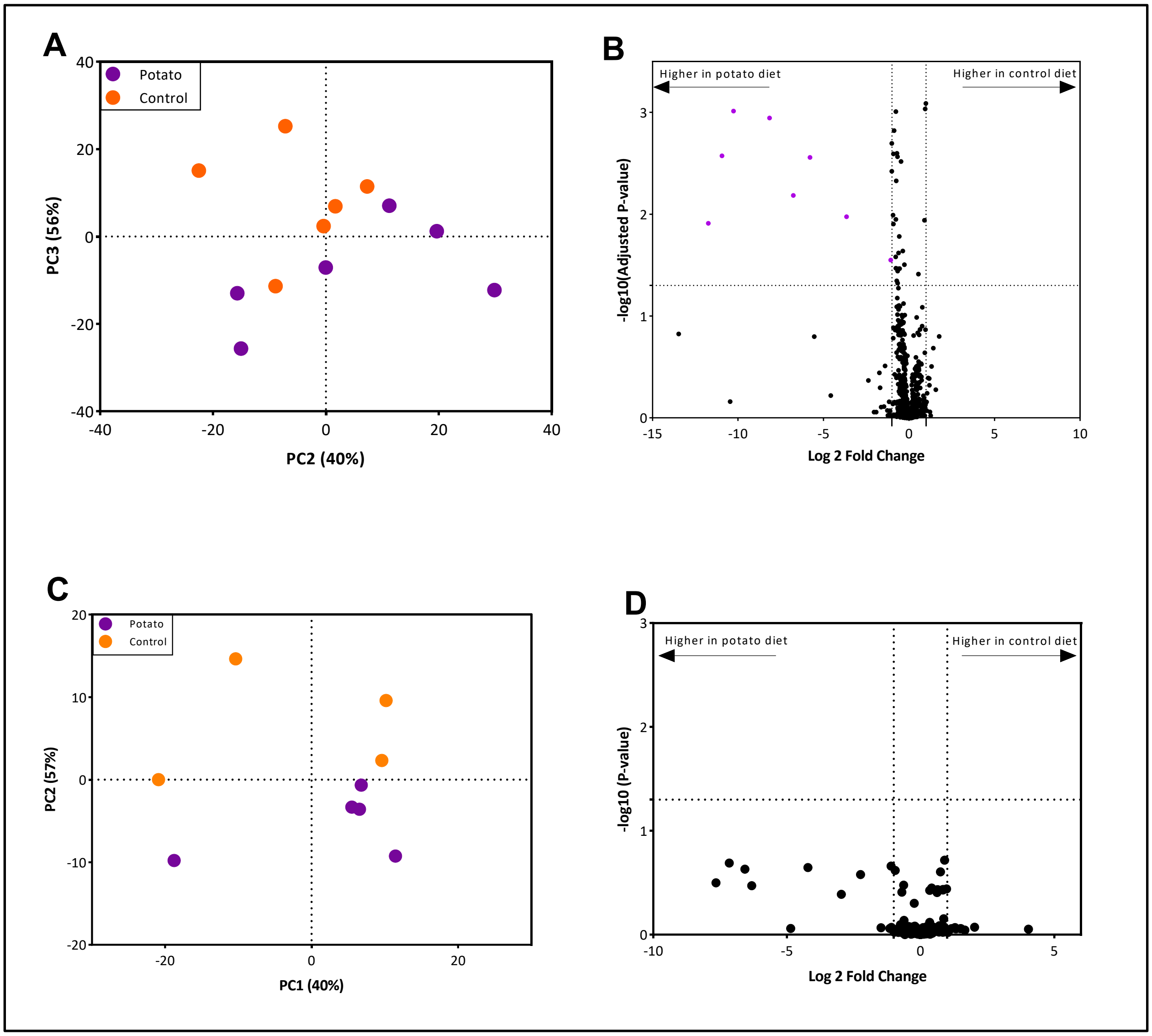


**Figure 3.6.** Obese metabolites variation potato vs control diet. Variation in liver and serum metabolites in obese animals on the potato vs control diet. Principal components analysis (PCA) of liver (A) and serum (C) metabolites in obese animals. Volcano plots of liver (B) and serum (D) metabolites. Purple points represent metabolites that are higher in potato diet (fold change $\geq 2$; adjusted $P \leq 0.05$).

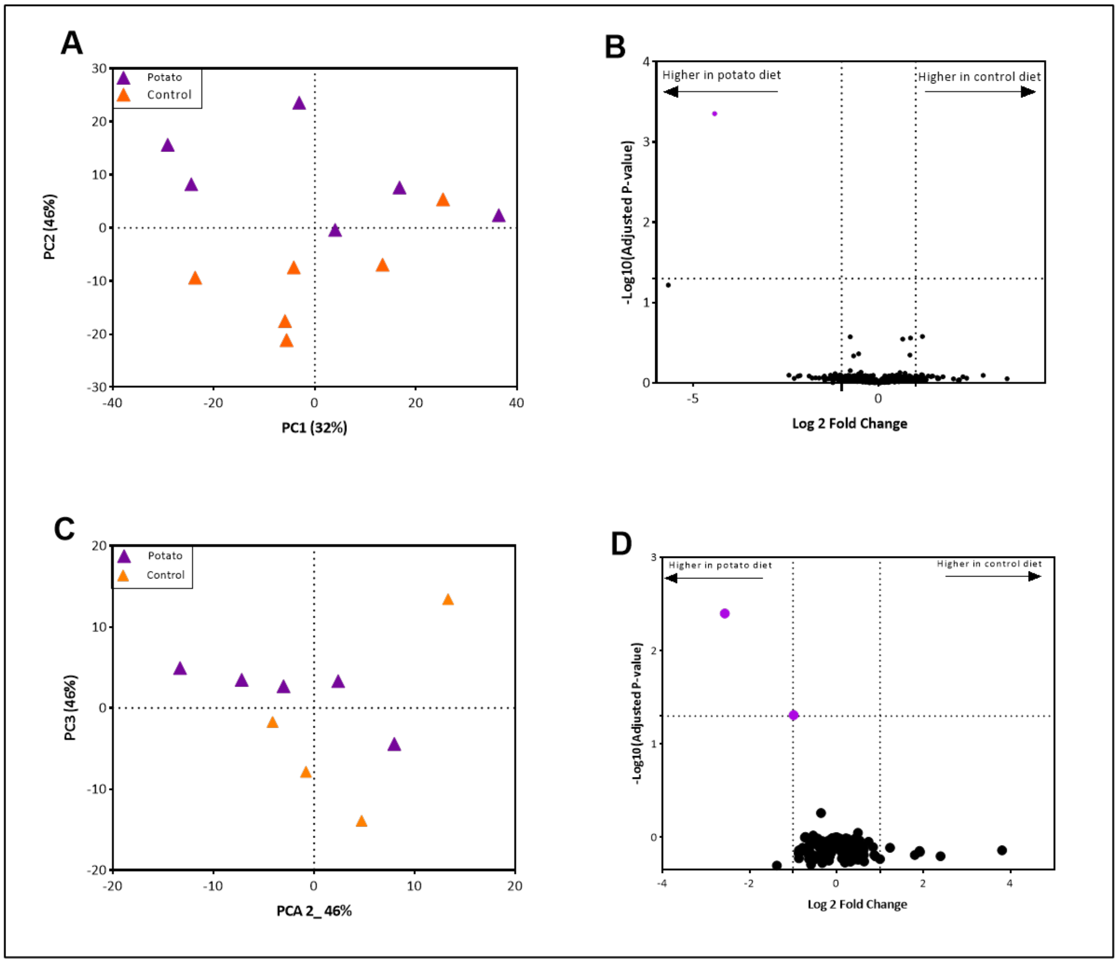


**Figure 3.7.** Lean metabolites variation potato vs control diet. Variation in liver and serum metabolites variation in lean animals on the potato =vs control diet. Principal components analysis (PCA) of liver (A) and serum (C) metabolites in lean animals. Volcano plots of liver (B) and serum (D). Purple points represent metabolites that are higher in potato diet (fold change ≥ 2; adjusted P ≤ 0.05).

Beside the overall variation in metabolite classes described above, a several individual metabolites demonstrated interesting difference between the potato and control diets (Figure 3.8). Examples include cholesterol sulfate, helilupolone, and tomatdine (detected in liver tissue) and arachidonoyl-dopamine (NADA, detected in serum).

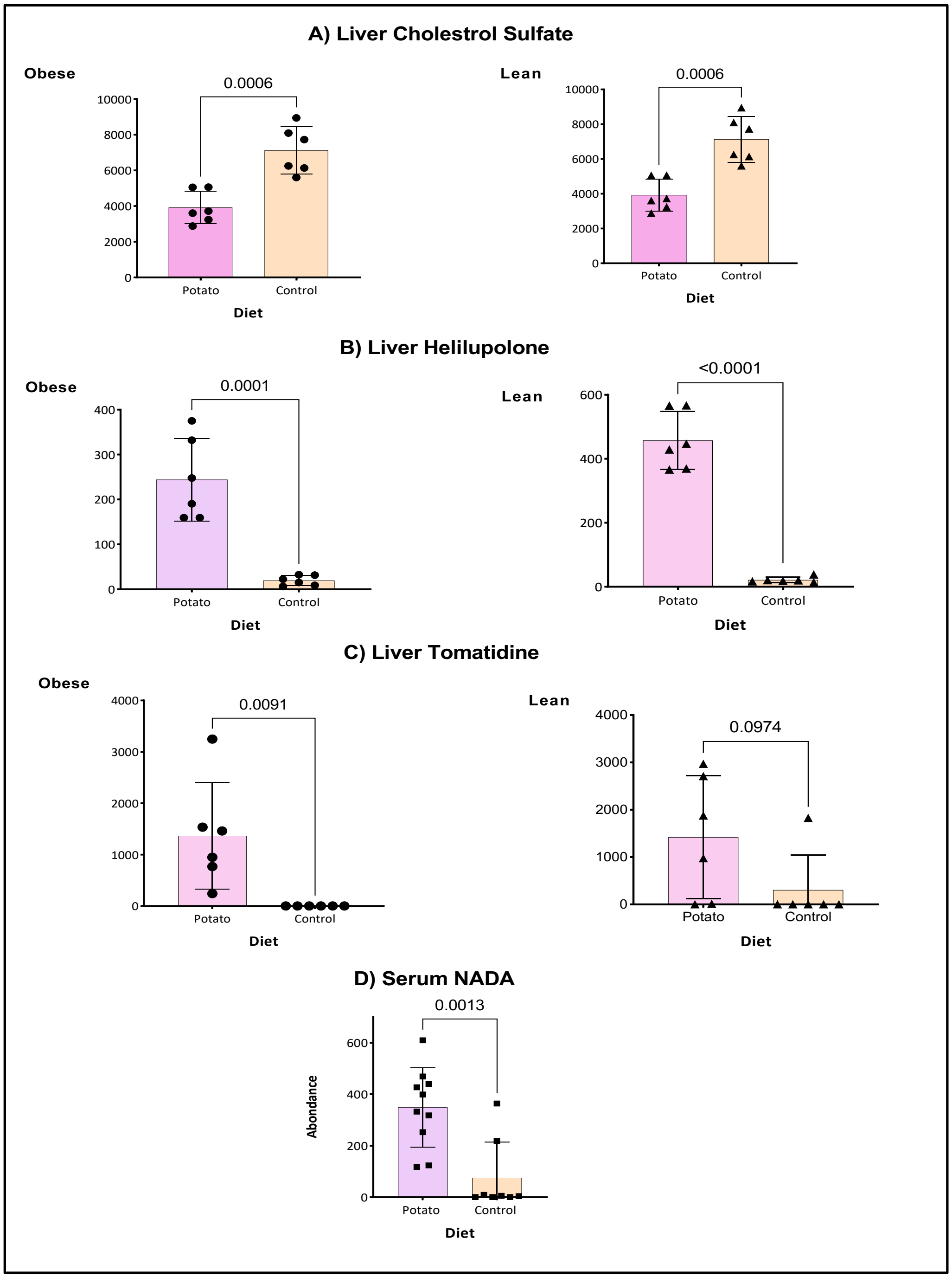


**Figure 3.8.** Relative quantitation of select liver and serum metabolites in animals on the potato and control diets. A) Cholesterol Sulfate in liver of obese and lean animals. B Helilupolone in liver of obese and lean animals C) Tomatidine in liver of obese and lean animals and NADA in the serum of relative quantitation represents the normalized spectral abundance. Data are expressed as the mean ± SE; n=6 or 10/ group. Statistical analysis was performed between potato and control diet using a student t-tests.

## 3.5. Discussion

My study demonstrates that a high phenolic potato diet resulted in a food intake reduction leading to weight loss in both obese and lean animals compared to animals on a control (non-potato) diet. Specifically, obese animals, who tend to over-consume food due to the deficiency in leptin, did not consume as much compared to their control group when put on a high phenolic whole potato diet. The lean animals, who are not leptin-deficient and tend to eat normally, also lost weight when they received a potato diet as compared to the control diet.

There is an increasing body of evidence supporting the importance of plant-based diets, which are high in phytochemicals, to improve the maintenance of whole-body metabolism and immune function. Plant food products are complex, providing a mixture of macro-/micro-nutrients and phytochemicals (e.g., phenolics), all of which influence not only appetite but also other metabolic pathways involved in obesity and CMD. Plant phenolics have been drawing considerable attention as natural, medicinal, and pharmaceutical products for appetite suppression and weight management (Molan et al., 2008, Bajerska et al., 2016, Coe and Ryan, 2016, Castro-Barquero et al., 2018). For example, it has been demonstrated that supplementation of drink or food with polyphenols decreased hunger and appetite in healthy males and females (Coelho et al., 2021, Coe et al., 2013, Garvey et al., 2017), although the exact mechanism of this effect is still not understood. However, it is known that phytochemicals, specifically phenolics, have a complex chemical structure and that they can be consumed and transformed by both the host digestive system and the gut microbiota. These processes can also be influenced by the presence or absence of macromolecules such as proteins or carbohydrates. The enteroendocrine system has been proposed to be a potential pathway for phytochemical metabolism by induction of satiety through the release of gastrointestinal peptides, such as cholecystokinin (CCK), glucagon-like peptide-1

(GLP-1) and peptide YY (PYY), from enteroendocrine cells in the small intestine(van Avesaat et al., 2016, Smeets and Westerterp-Plantenga, 2009). The effect of gastrointestinal (GI) hormones, alone or in synergy, on the regulation of food intake and glucose homeostasis has been well established. Specifically, they have been shown to stimulate glucose-dependent insulin secretion and insulin biosynthesis, inhibit glucagon secretion, and reduce the rate of gastric emptying which inhibits food intake by triggering hypothalamic neuronal satiety signals (Irwin et al., 2015, May et al., 2016, Pathak et al., 2018, Song et al., 2019, Kjaergaard et al., 2019).

Another component of the potato diet that could be involved in satiety, is protease inhibitors (PIs). Gastrointestinal hormones are degraded by proteases like trypsin, and PIs deactivate these proteases allowing for greater GI satiety hormone action. The total protein content of potato is comprised of about 50% PIs, and consumption of potato protein extracts has been demonstrated to reduce appetite and total caloric intake in both rodent models and humans (Komarnytsky et al., 2011, Chen et al., 2012, Ku et al., 2016, Zhu et al., 2017). As such, potato protein extracts have been used in several plant and protein-based weight loss supplements (Flechtner-Mors et al., 2020). Daily oral administration of a potato PI extract was shown to greatly increase serum CCK levels within rats in a dose-dependent manner (Komarnytsky et al., 2011, Serquiz et al., 2016). Another study showed that consumption of 15 mg of potato PIs one hour prior to the breakfast resulted in a significant increase in postprandial serum CCK levels within healthy females compared to subjects receiving the placebo (Zhu et al., 2017). The effect of PIs on CCK production has also been examined in vitro, using CCK-producing enteroendocrine cells, which has demonstrated a strong induction of CCK release upon treatment with PIs isolated from potato (Komarnytsky et al., 2011, Nakajima et al., 2011, Chen et al., 2012).

I also observed an impact of diet on animal weight. The obese leptin-deficient mice (obese group) were heavier throughout the study, as expected. However, the obese mice who were on the potato diet lost significant weight as compared to obese animals on the control diet. This could be attributed to the corresponding lower food consumption of the animals on the potato diet but there also may be an impact on metabolism that results in weight loss. Clinical studies have shown a decrease in body weight, without changes in calorie intake when supplementing food with phytochemicals (phenolics). Baur showed that the addition of 0.04% phenolics (resveratrol) to a high-fat diet slightly reduced the body weight in healthy mice after 75 weeks (Baur et al., 2006). Another clinical trial showed that enrichment of coffee with chlorogenic acid induced a reduction in slight to moderately overweight volunteers after 12 weeks (Thom, 2007). Other mechanisms have been linked to the effect of the phenolic compounds on digestion and metabolism. For example, clinical studies revealed that polyphenols have the potential to bind to starch molecules in foods, slowing the rate of starch breakdown (Gonthier et al., 2003) or inhibiting the intestinal alpha-glucosidase activity (Tadera et al., 2006). Polyphenols such as resveratrol have been demonstrated to improve insulin sensitivity, stimulate AMP activated protein kinase (AMPK) and lower serum glucose and insulin levels after 2 g kg-1 oral glucose gavage (Baur et al., 2006).

To gain insight on the impact of the high phenolic potato diet on host metabolism I utilized a non-targeted metabolite profiling approach. The metabolome represents the collection of small molecules (molecular weight < 2 kDa) in a biological system (e.g., serum or tissue), which reflects of individual genetic makeup and environmental factors (e.g., diet). Nutri-metabolomics is a term used to describe the application of metabolomics in nutrition-based studies (e.g., for the identification of dietary intake biomarkers) (Guasch-Ferre et al., 2018).

To my knowledge this is the first study to evaluate the impact of a cooked whole potato diet on metabolism in an animal model for obesity. I observed a significant modulation of metabolism (represented in serum and liver metabolites) in animals on the high phenolic whole potato diet compared to those on the control diet and this modulation was different in obese vs. lean animals. My findings are aligned with several published studies which have also investigated the correlation of serum and liver metabolism with obesity metrics (Beyene et al., 2020, Gu et al., 2020, Feldman et al., 2017, Wiklund et al., 2014). For example, my observation of increased certain triglycerides (TGs) in obese animals compared to lean (Figure 3.4. A), correlates with other studies that have shown high level of TGs are associated with obesity (White et al., 2017, Mills et al., 2019, Renault et al., 2017, Ho et al., 2016).

The metabolite profiles were also observed to be influenced by diet within the obese and lean animal groups (Figs 3.6 and 3.7) This result aligns with previous metabolomics studies that have shown variation in serum metabolites resulting from different subject diets. For example, Barton et. al. showed that in a human isocaloric cross over study with low and high glucose index diets, serum metabolites varied by up to 22% (Barton et al., 2015). In another cross sectional study, metabolite profiles of 1000 participants revealed an association between diet and serum metabolite composition, regardless of genotype (Esko et al., 2017).

One of the specific compounds observed to be significantly different in serum from animals on the potato diet is arachidonoyl-dopamine (NADA), (Figure 3.8.4.). Endocannabinoids are comprised of arachidonic acid-derived fatty acids (e.g., Arachidonoyl-dopamine (NADA)) derivatives of long-chain unsaturated fatty acids, with a neuroactive lipid (Novosadova et al., 2021, Price et al., 2004). The potential routes for NADA biosynthesis have been linked to tyrosine metabolism via either dopamine or NA-tyrosine (Huang et al., 2002, Hu et al., 2009). The mammalian endocannabinoid system controls multiple physiological functions by activating two distinctive receptors belonging to G-protein coupled receptor (GPCR) family, named Cannabinoid Receptors (CB). These receptors are expressed throughout the brain (CBR1) and on immune cells (CBR2) (Amaya et al., 2006, Sancho et al., 2004, Matsuda et al., 1990). Activation of both receptors have been linked to several type of neuronal activity such as pain (Luongo et al., 2017, Calignano et al., 1998), memory processing (Wotjak, 2005), and regulation of motor activity (Palomo-Garo et al., 2016, Orr et al., 2021). The endocannabinoid system also provides immunomodulatory action through its involvement in hemostasis and release of multiple biologically active substances such as inflammation mediators and cytokines. More specifically, NADA is associated with anti-inflammatory action and regulating the transcription factors (TNF) and cytokine release by T-cells. It can also inhibit the NF-kB signaling pathway which is known to play a critical role in the immune response (Sancho et al., 2004, Nagamoto-Combs and Combs, 2010, Sancho et al., 2005). NADA has also been shown to have neuroprotective activity in neurotoxic conditions through antioxidant properties (Marsicano et al., 2002, Bobrov et al., 2008, Vuolo et al., 2019, Paloczi et al., 2017, Ahmed et al., 2021). NADA has been introduced as a non-steroidal anti-inflammatory drug which inhibit cyclooxygenases, leading to a decrease in the synthesis of pro-inflammatory lipid metabolites thereby decreasing inflammatory and inflammatory pain (Arnold et al., 2021, Farkas et al., 2011, Price et al., 2004, Amaya et al., 2006). Antioxidant activity of NADA has been evaluated *in vitro* and shown to have a higher metal chelating activity than the other phenolic and flavonoid compounds (Huyut et al., 2017). The antioxidant property of NADA has been demonstrated by the survival of human neurons under oxidative stress conditions (Novosadova et al., 2021). The effect of NADA is not limited to neurons, as cannabinoid receptors have been detected in human endothelial cells with all the known endocannabinoid metabolic enzymes (Wilhelmsen et al., 2014). Increased levels of NADA have been shown to result in a reduction of inflammation, improvement of human vascular tone maintenance, and to exert a vasorelaxant effect. (Wilhelmsen et al., 2014, Bobrov et al., 2008, O'Sullivan et al., 2004, O'Sullivan et al., 2009).

I also observed decreases in serum cholesterol (cholesterol sulfate) in obese animals who were on the potato diet compared to the control (Figure 3.8.1. A and B). This result likely reflects cholesterol biosynthesis resulting from tissue leakage into circulation, depending on the activity of the cholesterol synthesis pathway. The clinical levels of serum cholesterol sulfate are known to be influence by diseases like hypercholesterolemia and T2D (Sun et al., 2019, Li et al., 2021). Though factors such as exercise and fasting can decrease serum cholesterol levels(Cho et al., 2019). Jiménez-Girón et. al. reported an increase of cholesterol sulfate in the fecal matter after consumption of a high phenolic drink (red wine) and proposed that polyphenols found in the red wine were inhibiting the absorption of exogenous cholesterol and lipids in the small intestine (Jiménez-Girón et al., 2015).

Helilupolone was detected exclusively in the liver of both obese and lean animals on the potato diet (Figure 3.8.2. A and B). To my knowledge, there is the first report of the detection of this dihydrochalcone in potato. To date there are only limited reports of presence of this dihydrochalcone in leaf and flower extract of Helichrysum (Jovanović et al., 2020, Vujić et al., 2020).

Another interesting observation was detection of tomatidine in the liver of both obese and lean animals on the potato diet (Figure 3.8.3 A and B). Tomatine is a glycoalkaloid which has been reported in tomato and to our knowledge this steroidal alkaloid has not previously been detected in potato. Tomatidine has shown broad bioactivity *in vitro* such as inducing apoptosis, attenuating the proliferation of cancer cells (Yan et al., 2013, Huang et al., 2015a), and anti-inflammatory (Kuo et al., 2017) and anti-viral activity (Troost et al., 2020). More recently, there is evidence that this compound has a positive effect on lipid accumulation, mainly through activation of the AMPK pathway and regulation of lipid metabolism (Wu et al., 2021, Kusu et al., 2019) as described above. For example, mice on a high fat diet who receive tomatidine twice per week for 12 weeks lost weight and had significantly lower serum total cholesterol (Wu et al., 2021). However, I did not encounter any other reports of tomatidine detection in liver. As with all of the compounds detected in our study, annotation is presented at a Level 2 confidence (putative) based on matching to an external spectral database. Confirmation of the metabolite annotation would require additional experimentation using an authentic standard. These annotations are based on spectral matching to a database and not to a standard so this is a putative identification that would need to be confirmed with an authentic standard, in future research.

Taken together, my results provide valuable information to help consumers and stakeholders understand the nutritional potential of potatoes. Unfortunately, potato has been vilified by consumers and nutritionists as a starchy food with high glycemic index (GI). Some official websites have actively encouraged the reduction of potato consumption, to reduce heart disease and improve weight loss. This narrative is derived from the incomplete understanding of the GI, insufficient understanding of the starch composition in potato, and even misinformation regarding the healthy dietary pattern. Today, it is known that these arguments are in contrast with the results of several research studies showing that potato as a whole food can in fact reduce appetite by elevating the satiety hormone. The USDA guidelines are transitioning to a different definition of a healthy diet (USDA and USDHHS, 2020) and the potato industry needs to take advantage of this opportunity to present its case for potatoes to appropriately position this food in future health dietary guidelines. Future studies are needed to investigate the complete profile of potato compounds, including small and big molecules, and specifically prebiotics. Potatoes contain multiple metabolites that have been extensively studied in other food sources for their prebiotic activity. Prebiotics in potato include small molecules (e.g., phenolics), protease inhibitors, soluble fiber (e.g., oligosaccharides) and insoluble fibers (e.g., pectin).

In the long term, the results from this preclinical study along with future research on health promoting compounds in potato will directly enhance potato breeding strategies to improve the supply of quality food for consumers. Developing potato cultivars that can be used as a vehicle to provide human nutrition and fiber needs, as well as sustain the economic viability of potato growers and their industry stakeholders would represent a significant step forward in addressing global food security.

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# CHAPTER 4:

# GROWER DECISION MAKING FACTORS IN ADOPTION OF SPECIALTY CULTIVARS: A CASE STUDY OF POTATO

## 4. 1. Introduction

Potato is the most consumed vegetable crop in the United States (U.S.) and is critical the U.S. agricultural economy. In 2020, the U.S. fresh and processed potato market was valued at $4.3 B (USDA and NASS, 2020), and in the global market, the U.S. had $1.7 B in exports as the fourth largest producer after China, India, Russia, and Ukraine (USDA and ERS, 2021, AgMRC, 2018). The U.S. state of Colorado is among the top sixth potato producers by sales, and the second top shipping state in the U.S., with a value of $210 million in 2019 (USDA and NASS, 2020, USDA et al., 2020). In Colorado, most potato production occurs in the San Luis Valley (SLV); $209 of the $210 million (Hill and Pritchett, 2016). The SLV is geographically optimal for potato production for its high elevation, nearly complete enclosure by surrounding mountains and plains, and uniquely high sandy soils.

In agriculture, research, and innovation function to continually improve food crops for yield, disease resistance, and resilience to grow in challenging climates. A major player is plant breeding, the process of crossing plants to introduce new combinations of genetics in the food system, and the result is a new cultivar (sometimes referred to as a crop "variety"). Most cultivars that are released each year are minor variants of the already established genetics, usually with small changes such as better yield, disease resistance, or processing traits. However, plant breeding operations often concurrently breed for "specialty" cultivars (SCs). These cultivars are notorious for lesser yields and with industry-specified quality traits (e.g., shape, density), but excel at value added traits (Swarup et al., 2021, Ebert, 2020, Bradshaw, 2019). In potatoes, a novel value-added trait is related to human health. Most common potato lacks in color, but some SC potatoes are rich in anthocyanins (e.g., purple flesh cultivars) and carotenoids (e.g., dark orange flesh cultivars), and other phytochemicals with demonstrated preventative effects on cardiovascular disease and metabolic syndrome. (Mäkinen et al., 2016, Pihlanto et al., 2008, Kubow et al., 2014, Tsang et al., 2018). Each year, growers must decide in which cultivar to grow, and therefore this decision has an impact on the availability of a cultivar to consumers. This decision can be considered vital to public health as these cultivars are demonstrated to vary in traits important to human health (Chaparro et al., 2018, Bártová et al., 2015, Bártová and Barta, 2009, Subramanian et al., 2017, Pęksa et al., 2013).

Adopting a new approach (either using new technology or adopting a new crop) brings risk to the system and is therefore associated with complex psychological and economic factors. Previously identified factors that influence risk and adoption include socio-demographic (e.g., grower age, education level) (Kabii and Horwitz, 2006, Marangunić and Granić, 2015, Schaak and Mußhoff, 2018, Baumgart-Getz et al., 2012, socioeconomic (e.g., grower economic welfare, access to resources) (Pham et al., 2017, Ghimire and Huang, 2016), and circumstantial factors (social and neighborhood network) (Wang et al., 2020, Pham et al., 2017). As such, it is necessary to develop multi-factorial models to explain adoption in each agronomic system.

Here, I hypothesize that socioeconomic, social, and cognitive factors influence the decision-making process for growers to adopt specialty cultivars in potatoes. This was investigated within the SLV, Colorado, USA. Importantly, the SLV is also the location of the Colorado State University Potato Breeding and Selection Program, acting as the main source of potato research and innovation in this area. This program has released 28 cultivars since it was established in 1975, and many of the specialty cultivars have unique nutritional chemistries and improved human health traits. Therefore, this analysis was conducted to evaluate the barriers to growers adopting specialties generated from this center of innovation.

## 4. 2. Theoretical Framework

I integrated three established models of innovation to explain the decision-making process to adopt a new cultivar in potato. Here, I present a theoretical framework and central definitions of the model.

### 4. 2.1. Innovation.

Innovation is defined as a new object or idea applied to initiating or improving a product, process, or service (Hopkins et al., 2003). In the 1940s and 50s, early innovation approaches were linear models or “science pull” models in which the idea and innovation start from scientific and research organization, flow to technology (applied science), and then go to market (Godin, 2014, Barbieri and Álvares, 2016). Subsequently, with improvements in public wealth and knowledge, the evolution of consumer preferences made the innovation model more complex. In the mid-1960s, innovation stimulated the shift in perception towards the “market need-pull” model, since the market is the source of ideas that drive scientific operation (Rothwell, 1994, Barbieri and Álvares, 2016). Today, the innovation model is a mixed or coupled model. This model works by coupling the interaction between science and technology and the marketplace, with feedback loops. In these more complicated models, the idea and need are generated both inside and outside of the research firms with several go or kill decision points (Cooper, 2008, Barbieri and Álvares, 2016). Individuals and organizations involved in the development, manufacturing, sale and use on innovations, require interacting at these stages/gates. Missing these interactions in the process will cause the innovation to fail to perform (Cooper, 2008).

4. 2.2. Adoption and related models.

An adopter is defined as someone who is making the decision to invest their resources (e.g., time, money, operation) in innovation (e.g., technology or new idea). Adopting an innovation introduces risks to the system, and individuals react to this uncertainty in different ways. Many different theories and models in social and behavioral sciences may explain the innovation adoption process by consumers and producers. Rogers Diffusion of Innovation (DOI) model, as the most popular innovation model, explains that the adoption does not happen simultaneously with the innovation. A new idea (innovation) gains momentum over time and diffuses (or spreads) through specific populations or social systems, as individuals have different approaches and readiness towards it. The DOI model applied an adopter category divided people into five classes base on their adoption willingness and readiness (Fig 1). This model also explains the flow and adoption of innovation overtimes, as well as how the rate of adoption is influenced by several factors including communication channel, social system, attribute of innovation (e.g., comparability and complexity) (Fig 1) (Rogers, 2003, Rogers, 1995).

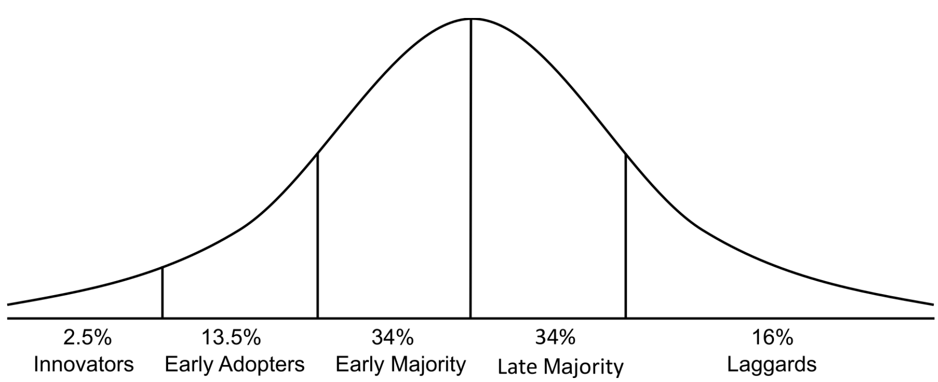


**Figure 4.1** Utilized Diffusion of Innovation model from Rogers (Rogers, 2003)**.** Five adopter categories and Innovators (2.5% of the population) who are the first group to adopt the innovation.

The second group is early adopters (13.5%) who follow by early majorities (34%) and late majorities (34%), and finally, 16% the laggards.

Adoption of innovation brings financial risk to the organization or farm, which makes growers uncertain whether to invest in the innovation. Some economic models have tried to explain the decision to adopt. For example, the Rational Expectations Hypothesis (REH) suggests that a grower has a rational self-interest in maximizing economic returns. Accordingly, expectations of future profit will play an important role in the grower's decision to adopt. In other words, growers will adopt the innovation if they believe total benefit exceed the implementation cost. Decision makers thus use the set of information (belief, knowledge, and experience), evaluate, and predict the outcome to decide if invest their resources (Muth, 1961, Evans and Honkapohja, 2001, Edwards-Jones, 2006). The socio-psychology variables are gaining more and more attention to use these insights to better inform policy design (Daxini et al., 2019, Wang et al., 2019a, Veisi, 2012).

Another theory, the Theory of planned behavior (TPB) was developed by Ajzen in the 1980s and has been applied to explain and predict the behavior of individuals. This model provides a socio-psychology structure which can predict intention with 40%-50% variance (Ajzen, 1985, Rose et al., 2018, Daxini et al., 2019, Veisi, 2012, Read et al., 2013, Armitage and Conner, 2001). Ajzen's model finds that human behavior originates from intention which may not always translate into behavior. This model explains that the intention to carry out certain behavior is determined by three central psychological predictors: attitude, subjective norm, and perceived behavioral control (Ajzen, 1985). The degree to which execution of the behavior is evaluated positively or negatively (attitude = A), the perceived social pressure to engage or not in the behavior (subjective norm = SN) and the perceived own capability to successfully perform the behavior (perceived behavioral control = PBC), together lead to positive or negative intention to perform a behavior (Wauters et al., 2010), explained in detail below. The TPB has been applied to explain and predict the adoption of an innovation and decision-making process in: sustainable agricultural and clean technology (Veisi, 2012, Zeweld et al., 2017, Read et al., 2013, Adnan et al., 2018), land management practices (Senger et al., 2017, Wang et al., 2019a), natural resource management (Price and Leviston, 2014), water management (Inman et al., 2018), animal welfare practices (de Lauwere et al., 2012), organic farming (Läpple and Kelley, 2013), and precision agriculture (Adrian et al., 2005).

4. 2.3. Attitudes and Behavioral Beliefs.

An attitude is a person's positive or negative feelings and evaluation of the perceived outcome and is a key behavioral and fundamental block of behavioral change. Behavioural beliefs (BB) are beliefs abehaviorbout the likelihood of a certain outcome (i) of the behaviour (b) and the evaluationof these outcomes (e) $(BB = \sum_{i=1}^{n} biei)$ (Wauters et al., 2010, Senger et al., 2017, Borges and Oude Lansink, 2016). Several studies report attitude to be a significant predictor of intention to adopt; individual attitudes are found to differ across adopters or non-adopters (Martínez-García et al., 2013, Daxini et al., 2019, Inman et al., 2018). Several studies have pointed out the factors which can affect growers' attitudes, including a grower's knowledge and experience with the new technology or innovation, their age, and education (Adedeji et al., 2013, Ngokkuen and Grote, 2012, Price and Leviston, 2014, Jongeneel et al., 2008, Vanslembrouck et al., 2002, Szakály et al., 2019). Although attitude is not sufficient to predict behavior, normative beliefs (function of the subjective norm) and perceived behavior (function of control beliefs) are other control components that influence adoption.

4. 2.4. Subjective norms.

Subjective norms (SN) encompass individual perceptions and beliefs about the views of others (called reference group j), regardless of whether a behavior is considered normal or positive compared to what peers are doing. In a social system or network (e. agricultural society), members tend to consider the perspective of other members and related groups when forming their own attitudes towards a given behavior (Matuschke and Qaim, 2009, Price and Leviston, 2014, Daxini et al., 2019, Pham et al., 2017, Herforth et al., 2015). Subjective norms determined by normative beliefs (the nj X mj), which are the normative expectations of reference group (nj), and the motivation (m) to comply with the opinion of these referents to carry out the behavior ($SN = \sum_{j=1}^{n} njmj$) (Wauters et al., 2010, Senger et al., 2017). Social networks influence and drive the belief and behavior by reflecting on the consequences of that behavior on others. Several models have been developed to explain determinants of social influence on individual behavior (e.g., theory of normative social behavior, structural theory of social influence, social influence network theory) (Rimal and Real, 2005, Bandura, 1977). A grower's network has been found to significantly affect their intention to adopt the new practice (Price and Leviston, 2014, Lambert et al., 2007, Siebert et al., 2006, Blackstock et al., 2010, Deressa et al., 2009, Pham et al., 2017). In addition, factors such as education level, age, economic status, network size, participation in social activities, and interactions with others impact their normative beliefs (Lastra-Bravo et al., 2015, Pham et al., 2017).

4. 2.5. Perceived Behavioral Control.

Perceived Behavioral Control (PC) is an individual's perception of their capacity to conduct successful performance and behavior. It is the belief of the ease or difficulty for an individual to implement a particular behavior, or the extent to which they feel in control of the decision-making process (Price and Leviston, 2014, Rose et al., 2018, Borges et al., 2014). Belief about the presence of different factors (k) that can facilitate or inhibit the execution of certain behavior (c). The control belief also results from the perceived power of the ($k_{th}$) factor to facilitte or inhibit the behavior (p) ($PC = \sum_{k=1}^{n} ckpk$) (Borges et al., 2014, Senger et al., 2017, Wauters et al., 2010). A grower's possession of knowledge and training to use the innovation are factors that influence their belief in the ability to control and manage risk (Inman et al., 2018, Kuehne et al., 2017). Growers integrate and evaluate their ability to control the financial outcome, success, and risk of the innovation (Price and Leviston, 2014).

### 4. 2.6. Framework Developed Herein.

The increasing evidence shows that these attitudes and beliefs lead to a positive or negative intention to perform a behavior. The intention of a grower to adopt is higher if they evaluate it positively, believe that others think they should perform it, and perceive it to be easy to perform and is under their control (Read et al., 2013, Veisi, 2012, Michie et al., 2008). Through literature review, our analysis of TPB suggested it has not previously been used to analyze and predict grower adoption of a new specialty crop, as it is applied in this study, including in potatoes. Agricultural organizations are not a solitary decision-making entity in which individual socio-psychology factors can predict their decision-making process. Social and economic factors simultaneously explain the agriculture organization's decision and adoption status (Rose et al., 2018, Ingram, 2008, Mac, 2002, Marra et al., 2003). Changing the behavior and shifting the growers to adopt a new cultivar result from multiple motivations and drivers. Here, we constructed an integrative theoretical framework to address the objective of our study, Fig 2. We used Ajzen

TPB components: behavioral belief, normative belief, and perceived control (Ajzen, 1985, Ajzen, 1991) to explore grower attitude and intention to adopt. Acknowledging that other factors may contribute to adoption, and as Ajzen had mentioned that TPB is "in principle" open to inclusion of other predictors to capture other components which affect the adoption, we integrated social and demographic factors with behavioral components (Burton, 2004, Burton, 2014, Ajzen, 1991).

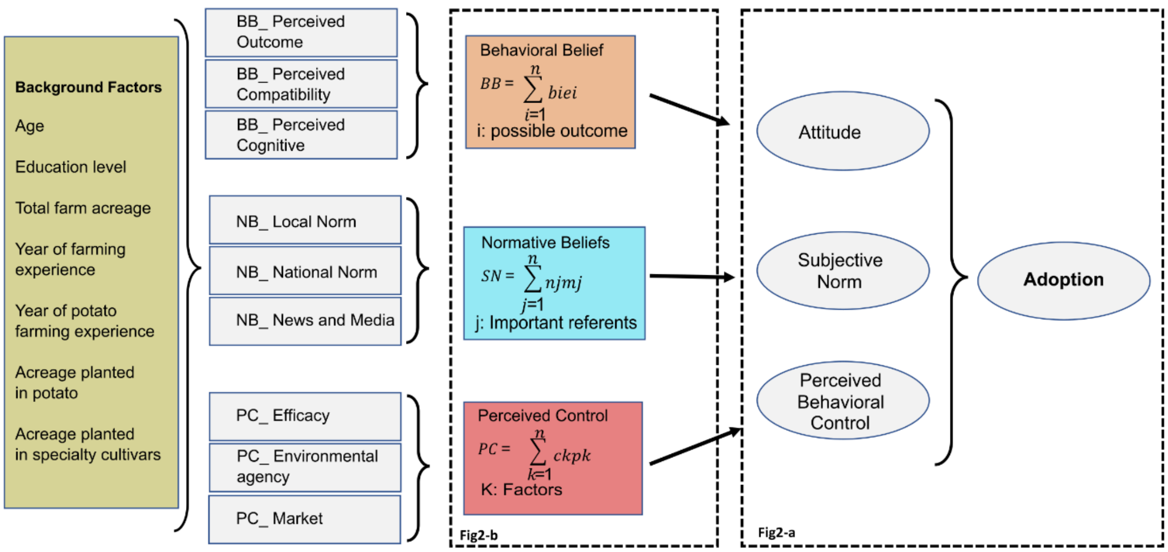


**Figure 4.2.** Theoretical Framework for Adoption of Potato SCs**:** Background factors collected for analysis of adoption in potato to model behavioral belief (BB), normative belief (NB) and perceived control (PC). (a): Three constructs of Theory of Planned Behavior (TPB) model, adapted from Ajzen (Ajzen, 1985). (b) Adaptation of Borges et al (2016) and Wauters et al (2010) models shows that the aggregative effect of behavioral belief, normative belief and perceived control on the attitude, subjective norm and perceived behavioral control.

## 4.3. Experimental Procedure

### 4. 3.1. Study Area and Procedure.

The study was conducted in the San Luis Valley (SLV), in south-central Colorado, USA. This is a high alpine valley with sandy soils, is part of the Rio Grande Rift, and stretches approximately 122 miles by 74 miles, surrounded by the San Juan Mountains on the West and the Sangre de Cristo Mountains on the East. Farming and ranching are the main sources of income for the San Luis Valley, and potatoes comprise 92% of the crop produced (Dubinsky et al., 2019, Hill and Pritchett, 2016). The SLV represents the third largest potato growing region in the United States.

The study was conducted in two steps (Fig 3). First, an interview was performed to contextualize the components of our theoretical model based on the condition of potato growers in SLV. Second, a subsequent survey was conducted to investigate the factors initially formed via interview and subsequent literature review. The survey included questions to model the following factors: (A) background (farm and grower demographic and characteristics); (B) behavioral beliefs (outcome, compatibility, and cognitive beliefs); (C) normative beliefs (local, national, news and media); (D) perceived control (efficacy, environment, market).

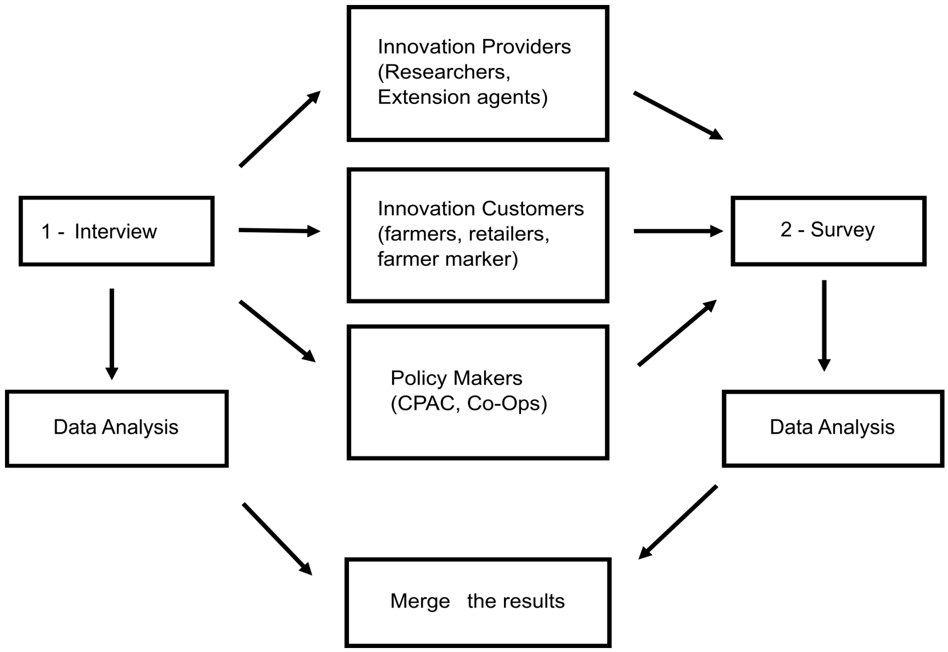


**Figure 4.3.** Experimental Design to collect and analyze qualitative and quantitative data. The first step in the procedure was an interview. The interview data was analyzed and used to generate the survey as the second step. Data from both the interview and the survey were merged for subsequent modeling.

### 4. 3.2. Interview.

First, an interview was conducted to understand potential economic and social constraints and opportunities. Three groups were established for preliminary interviews: 1) Innovation Users (growers, household food users, retailers); 2) Innovation Providers (researchers, scientists, extension agents); and iii) Policy Makers (local commodity groups, cooperatives). Interviewees were initially characterized based on the five categories/ groups of innovators to match the Rogers innovation graph (Fig 1). Semi-structured face-to-face interviews were conducted with 20 growers, with four from each group randomly selected to interview, via recorded audio, later transcribed, and analyzed. Questions were open ended and descriptive. These interviews were used to capture the important outcome (i), important referents (j), and factors (k) involve in grower's intention to adopt, using the Borges method (Borges et al., 2014, Borges et al., 2016).

4. 3.3. Survey.

A descriptive survey (open-ended, Likert scale, rating scale, single answer, multiple-choice questions) was designed by a panel of researchers at Colorado State University and was translated as descriptors and variable names in Table 1. The survey was initially tested on five growers and reviewed by the director of the local potato commodity board for content validity. The survey was administered in February 2019 with 80 potato growers responding, out of the 135 total potato growers in the SLV; 76 of the responses were complete and used in the analysis. The survey was administered on tablet computers in person using Qualtrics (QualtricsXM, 2019) at a local agricultural conference. The survey included four sections to investigate our hypothesis.

*A. Background factors.* Background factors were determined as grower age, education level, year of farming experience, year of farming potato experience, farm acreage, totthe al acreage of the farm planted in potato, percentage of the farm planted in SCs.

*. Behavioral belief (BB):* growers were asked to evaluate and rank their belief regarding planting SCs in three main categories. The first group of questions was directed towards perceived outcomes. Growers were asked if they think (even if they are not currently planted SCs or even never planted them) SCs have the same expenses but they bring higher yield and more profits to their operation. They also asked if they believe that SCs have a better flavor and if they are healthier, compared to conventional cultivars and they are more marketable (Table 1). To evaluate grower attitude toward cultivation, management, and storage of SCs Compatibility belief questions designed. Also, a group of questions intended to evaluate grower cognitive belief and their attitude toward future market and demand among consumers and industry for SCs.

*C. Normative beliefs (NB):* evaluated with 5-point Likert scale questions (extremely likely to extremely unlikely), growers were asked to rank how likely they are to rely on each reference group and information sources when deciding which cultivar to plant for the next year or next season. Refence groups were determined in the preliminary interviews and used to form data reported in Table 2, specifically i) local reference group (local university research center, extension center, local realtors and warehouses or industry) ii) national references (US potato, USDA, and other official ag websites), and iii) reference of news and media (news and social media).

D. *Perceived Control (PC)*: determined with ranking questions where growers were asked to rank the factors affecting their decision-making. I investigated the influence of different factors, defined in interviews to form data reported in Table 2), in three categories: i) Perceived Efficacy asked by ranking the influence of what their farm grew and sold last year, how easy and compatible would be using new cultivars and the characteristic of new verities regarding maintenance and storage. ii) Perceived Environment questions designed to assess the power of factors surrounding grower such as if the neighbor farm grew and sold specific cultivar, if they receive and informed of specific needs from special consumer or commodity and if their family like to eat a specific cultivar. iii) Growers perceived of their control over the market asked by the influence of, their own or their neighbor's, sale in the previous year or season, and the direct request they receive from various market sources.

**Table 4.1:** Survey translated to a description and corresponding independent variables.

| Variable Class | Variable Name | Description |
|---|---|---|
| Background Factors | Adopter | Planted specialty potatoes in 2018 (1 if yes, 0 if no) |
| | Specialty Prct | Percent of potato acreage planted in non-russet cultivar |
| | Year Farming | Years of total farming experience |
| | Year Potato | Years of potato farming experience |
| | T_Acres | Total farm acreage |
| | P_Acres | Total farm acreage planted in potatoes |
| | PrctAcresPotato | Acreage planted in potatoes divided by total acreage (P_Acres/T_Acres) |

| | | |
|---|---|---|
| | Education | Highest level of education that Grower completed (Less than high school=1, High school=2, Some collage=3, 4-year degree=4, Graduate=5) |
| | Age | As of December 31, 2018, what is grower age? - Year old |
| Market Channel | MC_W | Warehouses (1 if yes, 0 if no) |
| | MC_Chip | Chippers (1 if yes, 0 if no) |
| | MC_De | Dehydrators (1 if yes, 0 if no) |
| | MC_Ret | Retailers (1 if yes, 0 if no) |
| | MC_Expo | Export markets (1 if yes, 0 if no) |
| | MC_FM | Farmer market (1 if yes, 0 if no) |
| | MC_etc | Other (e.g., bulk) (1 if yes, 0 if no) |
| | MC_Industry | Chippers, Dehydrators, Export (1 if yes, 0 if no) |
| | MC_FarmerNitch | Farmer markets or export market, local consumers, retailers (1 if yes, 0 if no) |
| | MarketDiversity | Total number of market channels used by farm |
| Behavioral Belief (BB) Perceived Outcome (i) | Per_HighYield | Higher yields (True=3, Neither=2, False=1) |
| | Per_LowerCost | Lower cost of production (True=3, Neither=2, False=1) |
| | Per_MoreProfit | More profitable (True=3, Neither=2, False=1) |
| | Per_MoreMarket | More marketable (or subject to higher levels of competition) (True=3, Neither=2, False=1) |
| | Per_BetterTaste | Taste better (True=3, Neither=2, False=1) |
| | Per_Healthier | Healthier (True=3, Neither=2, False=1) |
| BB Perceived Compatibility (ii) | Less Disease | Less prone to pest and disease pressure (True=3, Neither=2, False=1) |
| | Per_LessLabor | Same labor requirements (True=3, Neither=2, False=1) |
| | Per_NotDifficultStor | Less difficult to store (True=3, Neither=2, False=1) |
| | Per_Certified | Lack certified standard (True=3, Neither=2, False=1) |
| | Per_KnownConsumer | Less known/appreciated by consumers (True=3, Neither=2, False=1) |
| BB Perceived Cognitive (iii) | Ati_Market | Over the next five years, the market for Colorado's specialty potatoes will increase |

| | | |
|---|---|---|
| | | (Strongly agree= 4, strongly disagree=1, Neither=0) |
| | Ati_Demand | There is a growing demand for specialty potatoes. (Strongly agree= 4, strongly disagree=1, Neither=0) |
| | Ati_Health | Consumers are more concerned about the health benefits of the crop (Strongly agree= 4, strongly disagree=1, Neither=0) |
| Normative Beliefs (NB) Local Norm (i) | T_Neib Farm | Neighbor growers (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| | T_CSU Ext | CSU Extension (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| | T_SLVResearch | SLV Research Center (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| | T_Industry | Commodity or Industry Organization (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| NB National (ii) | T_P USA | National websites (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| | T_USOrgNews | National websites, CDA, USDA (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| NB News and Media (iii) | T_S Media | Social Media (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| | T_News | Other websites and new outlets (extremely likely=4, somewhat likely=3, somewhat unlikely=3, extremely unlikely=1, neither=0) |
| Perceived Control (PC) Efficacy (i) | Influ_EasePro | Ease of production (including all aspects from planting to harvest) (most influential= 8, least influential= 1) |
| | Influ_Maint | Maintains character in storage (most influential= 8, least influential= 1) |

| | | |
|---|---|---|
| | Influ_etc | Other (etc., Disease resistant, Seed availability, Marketability, Water Use Efficiency) (most influential= 8, least influential= 1) |
| PC Environmental Agency (ii) | Influ_News | Information or news from the University or commodity organization (most influential= 8, least influential= 1) |
| | Influ_Like | What grower family like to eat or thinks tastes good (most influential= 8, least influential= 1) |
| | Influ_otherFarm | What other fellow growers like to plan (most influential= 8, least influential= 1) |
| PC Market (iii) | Influ_GrewPrev | What farm grew or sold in previous year (most influential= 8, least influential= 1) |
| | Influ_GrewNeigh | What neighbor farm grows (most influential= 8, least influential= 1) |
| | Influ_Req | Request from a retailer or specific market (most influential= 8, least influential= 1) |

4. 3.4. Empirical and Statistical Analysis.

In this study, the dependent variable (adoption status: Yes/No) was defined based on if the grower planted any potato specialty cultivars (SCs) in their farm in the previous farming year. Additionally, the level of the adoption is calculated as the percentage of SC acres planted to total acres planted.

A test of normality was run prior to further analysis. The data were analyzed using two different statistical platforms (GraphPad Prism, GraphPad Software, San Diego, California USA, and JMP Version 15, SAS Institute Inc., Cary, NC, 1989-2019) in two segments: descriptive statistic and inferential statistics. The mean, frequency, standard deviation (SD) and percentage were calculated for all famers and in both the adopter and non-adopter groups. For inferential statistics, first, we used Student's t-test, chi-square or Kruskal-Wallis to determine whether any of the differences between adopters and non-adopters are statistically significant (significance level of 0.05). Next, Spearman and Pearson correlation coefficients were calculated to assess the linear associations between independent variables and dependent variable (Adopters vs Non adopters). The binary nature of adoption (yes/no) allows for the opportunity to model the probability of adoption, depending on the other variables, in randomly selected sub-samples from population. A logistic binary choice model was utilized to provide a method for modeling adoption as a binary response variable, which takes values 1 (for adopters) and 0 (for adopters) and to estimate this probability and predict the effect of a variable on the responses. We used a logistic algorithm because it does not require linearity between dependent and independent variables and does not assume homoscedasticity. Wald $\chi 2$ statistics are used to test the significance of variable coefficients in the model. Each Wald statistic is compared with a $\chi 2$ distribution with 1 degree of freedom. The qualitative and quantitative data were merged in the analysis and interpretation phases of the study. This model predicted the probability of the response level (1 adopter or 0 for non-adopter) given the value of an independent variable (socio-economic factors, perceived attitude, norms, and controls ) (Press and Wilson, 1978, David W. Hosmer Jr. et al., 2013). Our logistic model was defined as the equation:

$$In[Pi/((1-\mathrm{Pi})] = \beta 0 + \beta 1\mathrm{X1i} + \beta 2\mathrm{X2i} + \dots\dots\dots + \beta\mathrm{kXki}$$

where the subscript i is the $i^{th}$ grower in the sample. P is the probability of that grower adopts the SCs and (1-P) is the probability that a grower does not adopt SCs. The regression of P on $X_i$s estimates the parameter of βk (1,2, …k) via maximum likelihood method. In logistic regression, the probability that all βs = 0 versus at least one β is not zero was tested, and probabilities were determined using the chi-square likelihood ratio test. The βs are considered a regression coefficient and indicate the effect of one unit change in the variable $X_i$ on the log of the odds when the other variables are held constant. The distribution probability of the difference between in the full model (containing all βs) and the reduced model (nested model) is calculated by the -LogLikelihood value. Therefore, the chi-square test was used to assess how independent variables (Table 1) improved the model fit. The chi-square probability of the difference between these models explains if the model is reliable or not. The improvement in the model fit with each added predictor is shown by statistical significance between the two models (Petrucci, 2009). The resulting classification matrix is a summary and can be used to calculate the specificity and sensitivity of the model. From the classification matrix, I calculated the percentage of the growers who are actually adopters and were correctly identified by our model (the sensitivity of the model).

### 4. 3.5. Consent and Ethical Statement.

This study was approved by Revised Human Subjects Regulations (Colorado State U IRB #19-8659H). The respondents were guaranteed about unrecognizability and confidentiality. They were also given the right to decline to answer the questions they were not comfortable. All participants gave written informed consent before entering the study.

## 4. 4. Results

### 4. 4.1. Interview and identification of theory of planned behavior components.

A semi-structured interview was conducted and identified the outcomes (i), important referents (j), and factors (k) as components of Theory of Planned Behavior (TPB) using the method proposed by Borges (Borges and Oude Lansink, 2016, Borges et al., 2014). From the interview I extracted five major groups for each component of the TPB. The outcomes that were important for the growers, and would affect their decision in planting specialty cultivars (SCs) were: (1) how the production process of a new cultivar (seeding to harvest) is going to be different from the conventional cultivars, (2) if by planting new cultivars they would need a different storage and packaging system (3) can their resources (financial and operational) handle the variation in production of these new cultivars (4) do these new cultivars have markets (5) Does planting new cultivars bring prestige and respect to their farm?

Growers were then asked whose opinion can positively or negatively affect their decision and indicated their social network and their relationship with local and national intuitional key players and policy makers play a significant role to motivate them to comply adopting a new cultivar. In this regard five groups based on important references (j) were identified (Table 2). Also, the growers' perception their control in producing new cultivars (a factor k) were demonstrated. These factors can facilitate or inhibit grower from executing specific behavior by giving the growers a positive or negative perceived over their capability of managing possible new circumstances. Table 2 shows the five factors (k) as (1) having a diverse operation which produces more than one product (i.e. potato seed, other crops, etc.) (2) having sufficient operation such as storage and ability to package (3) access to various markets (i.e. restaurant, growers market, etc.) (4) receiving direct request from specific buyers or markets (5) having sufficient knowledge of the benefits of the new cultivars.

**Table 4.2:** Perceived Outcomes (i), Important referents(j), and control factors(k) identified in semi-structured interviews.

| Outcomes (i) to measure behavioral beliefs ($b_ie_i$) | Important referents (j) to measure normative beliefs ($n_jm_j$) | Factors (k) to measure control beliefs ($c_kp_k$) |
|---|---|---|
| Production: disease resistance, water usage, etc. | Neighbor farm | Having a diversified operation |
| Efficiency of resource and input | Retailors, warehouses and Industry | Owning sufficient operation |
| Efficacy of Storage and package | Research and university | Having access to different markets for sale |
| Potential to sell to different market channel | Local agriculture departments | Knowledge regarding the new product |
| Social and professional prestige | Media and news | Knowledge of the sale and profits from previous years |

4.4.2. Survey respondent socioeconomic characteristics and associations to adoption.

Given the number of completed responses, we were confident that the views expressed by respondents in our 'survey sample' are broadly representative of those held by the population. Of the approximately 135 potato growers in the SLV, 80 growers completed the survey. A total of 4 surveys were excluded for incomplete responses (more than 80% of the survey was empty) and the final data set included information from 76 respondents. Characteristics of the respondents and the farm are shown in Table 3.

Here, SCs were defined as any potato other than white Russet potato (e.g., yellow, red, purple, fingerling, etc.), and adopters are defined as any grower who grow any SCs. Approximately 74% of the potato farms were dedicated to Russet (the conventional market class) and 26% to SCs. Specialty cultivars have been planted in 26% of the farms in the SLV, and adopters had devoted 43% (SD 34%) of their land to SCs. A total of 60% of the respondents were therefore classified as adopters (46/76). The mean age was 48 years old (SD = 15), and adopters were significantly younger with mean age of 42 years vs 56 in non-adopters (Kruskal-Wallis adjusted $P < 0.01$). Approximately 93% of the growers have education above the high school diploma with 23% having a college degree, 42% having a 4-year college degree, and 19% had a graduate degree. Education level also differed between adopters and non-adopters, with adopters having experienced higher levels (Kruskal-Wallis adjusted $P < 0.01$).

Farming experience widely varied in general (3 to 70 years, mean = 28, SD = 15) and for potato (1 to 70 years, mean = 24, SD = 17). Non-adopters compared to adopters have more years of farming experience (39 years vs 21 years) as well as potato farming experience (30 years vs 19 years). The mean farm size was 597 hectares (SD = 314, converted from acres reported I the survey), and approximately half of the farm was dedicated to grow potato (mean of 301, SD =

231). The adopters had significantly higher hectares of operations (Kruskal-Wallis adjusted P = 0.10), and they have significantly higher percentage of their land dedicated to potato (57% in adopters vs 42% in non-adopters with Kruskal-Wallis adjusted P < 0.01).

**Table 4.3.** Farm and Grower Characteristics

| Characteristics | | Obs | Mean | SD | Min | Max | Prob |
|---|---|---|---|---|---|---|---|
| Total farm size (hectares) | All | 76 | 597 | 314 | 51 | 1214 | |
| | Adopter | 46 | 682 | 328 | 51 | 1214 | |
| | Non-adopter | 30 | 464 | 239 | 129 | 963 | |
| | Adopter vs. non-adopter | | | | | | 0.01 |
| Land dedicated to potato (hectares) | All | 76 | 301 | 231 | 39 | 991 | |
| | Adopter | 46 | 383 | 226 | 45 | 991 | |
| | Non-adopter | 30 | 175 | 106 | 39 | 505 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |
| Farming Experience (years) | All | 76 | 28 | 15 | 3 | 70 | |
| | Adopter | 46 | 21 | 11 | 3 | 50 | |
| | Non-adopter | 30 | 38 | 15 | 10 | 70 | |
| | Adopter vs. non-adopter | | | | | | <0.01 |
| Potato Growing Experience (years) | All | 76 | 23 | 16 | 1 | 70 | |
| | Adopter | 46 | 18 | 11 | 2 | 40 | |
| | Non-adopter | 30 | 30 | 13 | 1 | 70 | |
| | Adopter vs. non-adopter | | | | | | 0.03 |
| Education Level (Likert scale 1-5) | All | 74 | 3.67 | 0.90 | 2 | 5 | |
| | Adopter | 44 | 3.95 | 0.86 | 2 | 5 | |
| | Non-adopter | 30 | 3.26 | 0.82 | 2 | 5 | |
| | Adopter vs. non-adopter | | | | | | 0.01 |
| Age (years) | All | 76 | 48 | 15 | 20 | 84 | |
| | Adopter | 46 | 42 | 13 | 20 | 65 | |
| | Non-adopter | 30 | 56 | 14 | 29 | 84 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |

### 4.4.3. Components of grower's attitude, subjective norm and perceived control toward planting specialty cultivar.

Behavioral Belief (BB) was comprised of three subgroups including perceived outcome, perceived compatibility and perceived cognitive (Figure 2). The perceived outcome of planting SCs were first identified in the interview and incorporated into the survey. The major trends were the belief that SCs have a higher outcome such as with marketability and profit (Table 4, mean = 1.82). Adopters had a higher positive perceived outcome towards the SCs compared to non-adopters (Kruskal-Wallis adjusted P < 0.01m Table 4). In the outcome questions, adopters and non-adopters demonstrated the same attitude toward taste and health attributes unique to SCs (Chi Square = 0.06 and 0.91). In the same category adopters believe that SCs are more marketable (Chi Square Likelihood ratio < 0.01) and can bring more profit to the operation (Chi Square Likelihood ratio = 0.01).

**Table 4.4** - Distribution of adopters and non-adopters by behavioral components

| Variable | Group | Obs | Mean | SD | Min | Max | Prob[b] |
|---|---|---|---|---|---|---|---|
| PC_Personal efficiency | All | 76 | 5.04 | 0.52 | 3.75 | 6.50 | |
| | Adopter | 46 | 4.90 | 0.51 | 3.75 | 6.00 | |
| | Non-adopter | 30 | 5.25 | 0.48 | 4.00 | 6.50 | |
| | Adopter vs. non-adopter | | | | | | 0.01 |
| PC_Environmental agency | All | 76 | 3.13 | 0.59 | 2.00 | 5.00 | |
| | Adopter | 46 | 3.23 | 0.62 | 2.00 | 5.00 | |
| | Non-adopter | 30 | 2.97 | 0.53 | 2.00 | 4.33 | |
| | Adopter vs. non-adopter | | | | | | 0.14 |
| PC_Market | All | 76 | 5.03 | 1.05 | 2.00 | 7.00 | |
| | Adopter | 46 | 5.29 | 1.07 | 2.00 | 7.00 | |
| | Non-adopter | 30 | 4.63 | 0.89 | 2.00 | 6.33 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| SN_Local norm | All | 75 | 2.37 | 0.81 | 0.00 | 4.00 | |
| Local norm | Adopter | 45 | 2.64 | 0.60 | 1.25 | 3.75 | |
| | Non-adopter | 30 | 1.97 | 0.91 | 0.00 | 4.00 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |
| SN_National norm | All | 74 | 1.58 | 1.13 | 0.00 | 4.00 | |
| | Adopter | 44 | 1.67 | 1.07 | 0.00 | 3.50 | |
| | Non-adopter | 30 | 1.46 | 1.23 | 0.00 | 4.00 | |
| | Adopter vs. non-adopter | | | | | | 0.03 |
| SN_ Media | All | 71 | 1.27 | 1.03 | 0.00 | 4.00 | |
| | Adopter | 43 | 1.28 | 0.90 | 0.00 | 3.00 | |
| | Non-adopter | 28 | 1.26 | 1.22 | 0.00 | 4.00 | |
| | Adopter vs. non-adopter | | | | | | 0.83 |
| BB_Perceived outcome | All | 72 | 1.82 | 0.36 | 1.00 | 2.66 | |
| | Adopter | 43 | 1.98 | 0.34 | 1.16 | 2.66 | |
| | Non-adopter | 29 | 1.59 | 0.26 | 1.00 | 2.16 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |
| BB_ Perceived compatibility | All | 73 | 1.70 | 0.38 | 1.00 | 3.00 | |
| | Adopter | 43 | 1.70 | 0.35 | 1.20 | 3.00 | |
| | Non-adopter | 30 | 1.71 | 0.42 | 1.00 | 2.80 | |
| | Adopter vs. non-adopter | | | | | | 0.99 |
| BB_ Perceived cognitive | All | 74 | 3.07 | 0.83 | 1.00 | 4.00 | |
| | Adopter | 44 | 3.31 | 0.62 | 1.00 | 4.00 | |
| | Non-adopter | 30 | 2.72 | 0.96 | 1.00 | 4.00 | |
| | Adopter vs. non-adopter | | | | | | < 0.01 |

**Table 4.4** - Distribution of adopters and non-adopters by behavioral components[a]

[a]PC: Perceived Control; SN: Social Norm; BB: Behavioral Belief

[b] Chi Square Likelihood Test for adopters vs. non-adopters

All respondents (adopters and non-adopters) believed that potato SCs are compatible with their traditional farming operation and equipment. Growers believed that the SCs are not more susceptible to disease, nor they do not need any special operation including labor and equipment.

Both groups believe that these varieties are not well known by consumers and within the market (41% of non-adopters and 58% of adopters with Chi Square = 0.24). Additionally, growers perceived cognitive was evaluated by asking if they think there is a growing demand for healthy and more nutritionally valuable crops. They were also asked if they think SCs have these health benefits and have the opportunity to have a larger market in next 5 years. Both groups were not sure if the market for SCs would increase in next five years, largely due to current certification problem and low consumer awareness of their benefits ( 47% of non-adopters and 52% of adopters with Chi Square = 0.06). Nevertheless, adopters had a significantly higher positive perceived cognitive (Kruskal-Wallis adjusted $P < 0.01$).

For Subjective Norm, questions in three subgroups qualified the reliance of grower on their important references and their information source. A grower's important references (j) were identified in the interview and shown in Table 2. Growers were asked to rank how likely are they rely on different sources of information with a Likert scale with 5 points, from strongly disagree to strongly agree. Trust to the local agricultural advisory groups and local peer growers were higher in adopters (Kruskal-Wallis adjusted $P < 0.01$). Factors of social media and national agriculture websites did not influence grower decision, though the adopters trended towards a higher reliance on national agricultural websites vs non-adopters.

For perceived control, these items were divided into perceptions of efficacy (personal efficacy), perceived environment, and perceived market to assess the ease or difficulty of performing the adoption behavior for the grower (Ajzen, 1987, Sutton, 2015). We asked growers about their perceived control over the cultivation and their experience with the market for SCs (perceived efficacy). Control on production process was an important factor for all growers when they decide what to plant. Adopters had higher positive perception of their personal efficacy for planting SCs (Kruskal-Wallis adjusted $P = 0.01$). I also asked how their perceived environment can control their decision (e.g., other grower's sales, their family). Both the adopter and non-adopter group decision was affected by what the neighboring farm could sell the year before and requests from industry or retailor. The market and the grower's perception of the market differed between the two groups (Kruskal-Wallis adjusted $P < 0.01$), although the difference between subcategories means for control efficacy of market were not significant. Further, retailers, chippers and dehydrators, and Farmer's Markets are the niches that growers also have access to in the SLV. Importantly, the data indicate that adopters utilized several of these markets, while non-adopters sold their products to only warehouses.

#### 4.4.4. Modeling the adoption status and decision-making process of growers.

The binary nature of adoption (yes/no) allows for the opportunity to model the probability of adoption, depending on the other variables, in a randomly selected sub-samples from population. A logistic binary choice model was used to estimate this probability and predict the effect of variable on the responses. The regression results of the Logit model include the coefficients ($\beta$), their standard errors, the Wald Chi Square statistic, connected P, and marginal probability (marginal effects) and are reported in Table 5. The statistical significance of individual regression coefficients ($\beta$s) was tested using the Wald Chi Square statistic reported in Table 4. The model demonstrates that several variables positively influence adoption behavior including local norms ($\beta = 2.87$ and $P < 0.01$), market diversity ($\beta = 1.16$ and $P < 0.01$), BB_Perceived Outcom ($\beta=1.77$, $P < 0.01$), PC_Perceived Market ($\beta=2.69$, $P < 0.02$), and BB_Perceived Cognitive ($\beta=14.74$, $p < 0.01$). While years of farming experience, specifically potato farming experience trended towards having a negative influence on adoption behavior ($\beta= -0.10$, $P < 0.06$).

The whole model was evaluated and found to be reliable (Table 6, -Log likelihood < 0.0001, $R^2 = 0.70$). The model's accuracy was also evaluated via a classification matrix (Table 7). The matrix shows the model can correctly classify a grower as an adopter with 90% precision and can identify non-adopters with 82% sensitivity. Thus, the overall model is significant, and the variables used in the model are together able to explain grower behavior regarding the decision to adopt potato specialty varieties:

$$\boldsymbol{log}\left(\frac{\boldsymbol{p}}{\boldsymbol{1}}-\boldsymbol{p}\right) = -50.26 + 1.16\,Market\ diversity + 2.87\ \mathrm{SN_{Local}}$$

$$+ 1.77\ \mathrm{BB_{Perceived}Outcome}$$

$$+14.47\ \mathrm{BB_{Perceived}Cognitive} + 2.69\ \mathrm{PC_{Percieived}Market} - 0.10\ \mathrm{Year\ Potato}$$

**Table 4.5:** Factors influencing the adoption of SCs determined by logistic regression*.

| Variable | β | Std Error | Wald Prob>ChiSq | Prob>ChiSq |
|---|---|---|---|---|
| BB_Perceived Outcome | 1.77 | 4.95 | < 0.01 | 0.03 |
| SN_Local | 2.87 | 1.21 | 0.01 | 0.01 |
| BB_Perceived Cognitive | 14.74 | 1.10 | 0.01 | 0.01 |
| PC_Percieived Market | 2.69 | 0.77 | 0.02 | 0.02 |
| Market Diversity | 1.16 | 0.55 | 0.03 | 0.03 |
| Year Potato | -0.10 | 0.05 | 0.06 | 0.06 |
| Intercept | -50.26 | 16.65 | | |

*PC: Perceived Control; SN: Social Norm; BB: Behavioral Belief

**Table 4.6.** Whole model test.

| AUC | $R^2$ | - Log likelihood (Prob>ChiSq) | Misclassification Rate |
|---|---|---|---|
| 0.975 | 0.70 | <0.0001 | 0.125 |

**Table 4.7.** Classification matrix to compare the actual vs predicted outcome.

| | **Actual** | **Predicted** |
|---|---|---|
| Adopter | 1 | 0 |
| 1 | 39 | 4 |
| 0 | 5 | 24 |
| Precision | 90% | |
| Sensitivity | 82% | |

## 4.5. Discussion

Here, I present an integrated theoretical framework that identified factors influencing a grower's decision-making process to adopt specialty cultivars (SCs). In this case study of potato, a grower's decision to adopt was shaped by their attitude, subjective norm, and their perceived behavioral control (Fig 2, Table 4). This study demonstrates how socioeconomic characteristics, farm characteristics, and behavioral factors contribute to grower decision-making related to planting a new SC. My results show that access to the market and having a secure mechanism for sale is the primary barrier to adopt SCs. Correspondingly, there is an association between willingness to plant new SCs and having access to several niche markets, beyond regular sources of sale such as warehouses. Interestingly, non-adopters were more reliant on their experience from a previous year cultivation and sale, while adopters were less influenced by previous experiences.

In this study, grower attitude was shaped by their assessment of compatibility, outcome, and their cognition. Both groups of growers agreed that SCs are compatible with their operating system. Yield and disease resistance have been mentioned as important factors for adopting new varieties (Adedeji et al., 2013). However, in this system, the SCs of potato in this local industry have acceptable yield and disease resistance. The positive correlation between farming experience (specifically potato farming) and perceived compatibility shows how experience enabled a positive attitude towards the management and cultivation of new SCs. The growers declared that even though SCs are usually smaller in size and sometimes are more sensitive to manage, they have enough experience to address modifications to cultivation.

Growers also were aware of unique SC traits of distinct flavor/color, cooking properties, and human health benefits. If a grower believes an SC has a unique property that consumers are looking for, they are more likely to consider planting those for their potential market. Both groups agreed that SCs have novel traits but believe that there is a significant lack of knowledge and awareness among consumers and industry that affect the marketability of these cultivars. This knowledge and awareness gap has resulted in a lack of certification and marketing for the new cultivars, which further increases the risk of not being accepted within the market.

Attitude differences between the two groups were evident in perceived cognitive and outcomes. Adopters believed that the market for potato is changing, and consumers are looking for specialized product. Growers (adopters) also believed that two SC traits will be attractive to consumers: smaller tuber size and larger variation in color, although they believed these cultivars have not been advertised and introduced to the market properly. In addition to the physical attributes of SCs, adopters believed the higher health benefits of SCs can be a significant factor to sale and lead to greater profit, which is consistent with other studies that demonstrate consumer value and willingness to pay for healthier products. For example, a study in Ohio (USA) found consumers were more willing to pay more for scientifically-backed claims of healthier tomato juice (Teratanavat and Hooker, 2006). In Europe, similar trends were observed for ‘ardioprotective foods in Germany (Hofmann et al., 2018), and paying more for healthier dairy products (Szakály et al., 2019, Bechtold and Abdulai, 2014). This increased willingness to pay for healthier food products is also demonstrated in staple plant foods such as rice (Cuevas et al., 2016), potato (Lacy and Huffman, 2016), and healthier potato chips (De-Magistris et al., 2016). Altogether, these studies support that consumer knowledge and awareness of health benefits of SCs can play an important role increased grower profits, grower adoption of new cultivars, and access of these cultivars for consumers within an industry.

I observed that year of farming experience has a positive correlation with growers perceived compatibility, but a negative correlation with their perceived outcome. Growers with more years of experience believed new SCs are not difficult to manage on their farm. Data reported by Danso-Abbeam (2017) along with Ojo (2014) show similar results, where adoption of new varieties of maize is higher among growers with longer years of experience in agricultural production (Ojo S. O. and I., 2014, Danso-Abbeam et al., 2017). Increased years of experience have also been observed in the studies regarding the adoption of new technology and farm management (Paustian and Theuvsen, 2017, Roberts et al., 2004, Reichardt et al., 2009). But in my potato study, years of farming in the area gave growers the perception that they know the market and they do not think the market is ready for these cultivars. This is within the broader trend of non-adopters having a negative perception of the SC market, leading them to believe that the margin of profit would not be worth the risk of adopting an SC. This may be attributed to that increased years of experience is linked to a stable source for sale (e.g., warehouses), which enhances the risk even more. This is interesting because this same uncertainty in the market is not a barrier for the adopter-growers, as they believe that market and consumers need change, and they are ready to meet the needs for this change.

There is growing evidence showing profound effects of social networks on individual behavior and a decision-making process. In a typical U.S. agricultural staple crop system, a grower's network includes their fellow growers, local universities and extension agents, local markets, and directly adjacent farms. The experiences shared within the network are an important driver of adoption.  In my potato study, this network was an important factor in influencing adoption of SCs. This is consistent with previous studies indicating that growers who are involved and exposed to training and workshops offered by university and extension services have a higher probability to adopt an innovation (Danso-Abbeam et al., 2017, Mmbando and Baiyegunhi, 2016, Mutari et al., 2021). The higher engagement of a grower with these information sources results in higher positive cognitive belief towards the distinct properties of SCs (e.g., color, health attribute) and their potential market. The adoption uncertainty can be overcome with the experience and information from trusted sources. In maize, improved and novel varieties were more likely to be adopted by growers who attended agricultural related seminar or conference, and have more contacts with extension (Mmbando and Baiyegunhi, 2016, Danso-Abbeam et al., 2017, Adedeji et al., 2013). In my potato study, it was interesting that the level of trust in an innovation was positively correlated with interactions between growers and university researchers/extension agents, and the ability to transfer useful knowledge to growers. Studies on adopting improved rice, barley, and potato also showed the quality of the information and expertise level of the extension agents influence a grower's trust in universities as sources of information and innovation (Adedeji et al., 2013) (Yigezu et al., 2015).

My research supports the need for university programs to closely work with growers to facilitate the adoption of new SCs and clarify their unique traits. Local grower-based organizations and networks have been also identified as factors that affect a grower's attitude towards the innovation (Mmbando and Baiyegunhi, 2016, Bruijnis et al., 2013, Borges et al., 2014). In general, grower-to-grower networking is as important as the grower's SC experience (Figure 1, early stage experience as 'innovators' and 'early adopters'), as it can give peers a perspective of the new situation. The influence of a peer grower's experience can improve grower's perception of the outcome. This is aligned with other research that shows how a grower's experience with a new technology or cultivar positively affects the overall adoption within a network (Choudhary and Rahi, 2018, Mutari et al., 2021, Suvi et al., 2021, Siebert et al., 2006). A grower's positive experience with either production or the sale of the new crop in a previous year increase the information and skills for others and increases the probability of adoption (Ghadim et al., 2005).

While both the adopter and non-adopter potato groups did not rely on the news of national agricultural websites, they had a heavy reliance on social media, and more significantly within the adopter group. This may be attributed to the premise that adopters use social media to connect with their consumers and obtain feedback from market. Social media can be a source of information for adopters to understand the consumer interest such as new diets trends and a corresponding new market. Further, along with the positive correlation between local networks and adoption, we see a negative correlation of adoption with years of farming (and potato farming) experience. Growers that were older and more experienced were more confidant in what they do and how they operate (i.e. they "figured it out"), and there is less contact and trust to local resources. This could be because younger and less experienced famers (adopters) tended to gather more information through different sources and evaluate a new market, while the older and more years in farming result in a stable situation that does to warrant high-risk activities.

A grower's perception of their ability to operate and manage the production of the new crop in their farm has been analyzed in several models as a predictor of adoption (Vasquez et al., 2019). In this potato study, I observed that a grower's perceived control varies, as adopters had higher perceived efficacy over the production to cultivate, harvest, store and more importantly sell the SCs. This belief in control over the cultivation and sale shows a correlation with growers of trust to local norms. Most of the positive correlation to local resources was towards the related university breeding program. This further supports how a university and extension service can empower growers to diversify their operation.

Another factor of adoption is age, and age has been shown in several studies as a barrier to adopt new technology or new product (Danso-Abbeam et al., 2017, Adedeji et al., 2013), but there is little understanding of why age matters. In our study, we found that that age correlated with a grower's trust in norms (local and national) and belief in avoiding risk.

The most important influence of a grower's perceived control is their belief in personal control over the market. Both groups were attentive to the request they had from the market (e.g., warehouses, local restaurants, Farmer's Market). In this potato study, the collective request from the local market reduced the risk of adoption. This is likely because it is essential for growers to know of the main buyers or a specific market is interested in buying their products (e.g., warehouses and retailors vs. restaurants, Farmer's Markets). Adopters had access to several niche markets, and this contrasted with non-adopters. This market diversity provides adopters with a tool to have a higher control over the new circumstances, even if the main market channel (warehouses) are not buying these new cultivars. Our data shows that among the adopters, younger growers seek more information and diverse channels of sale. Adopters with larger networks and increased market diversity gave them confidence that they can produce and sell the product to make a profit, even if the main market channel is not buying the new SCs. Further, growers that access niche markets need to transfer information about SCs and their distinct traits to those markets (e.g., Farmer's Markets, restaurants), and the learning of information negates a complete reliance on experience from past year's sales (i.e. thinking towards the future vs. the past). This contrasts with non-adopters, which tended to be heavily influenced by their neighbor's experiences and were more deterred from adopting new SCs by prior poor sales and experiences.

## 4.6. Conclusion

This study reveals the major barriers and influencing factors for how growers adopt specialty cultivars in the potato industry. University participatory breeding and extension is critical to facilitate adoption of new cultivars and is sufficient in transmitting knowledge of specialty potato, their unique traits, and potential markets. Potato growers have a strong awareness of new specialty cultivars and can manage them with little changes to regular farm operations. However, a broader awareness of the benefits of specialty cultivar traits, such as flavor and human health, is lacking throughout the market, and this is a critical step to promote adoption of new potato specialty cultivars by growers. Based on these data, the major recommendations for the potato industry include: i) increased dissemination of knowledge regarding unique traits to distributors and consumers; ii) continue and enhance agricultural extension services with knowledge of new specialty cultivars; iii) improve certification and packaging for specialty cultivars; and iv) promotion and improved focus on the utility of specialty cultivars in the market.

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# CHAPTER 5:

# SUMMARY AND FUTURE DIRECTIONS

According to the Centers for Disease Control (CDC), cardiometabolic diseases (CMD) such as cardiovascular disease and diabetes are the leading cause of death in the United States (CDC, 2019), which in turn, are strongly linked to obesity through the development of systemic chronic inflammation (Lumeng et al., 2007, DeBoer, 2013, Ndisang and Rastogi, 2013). Diet composition is known to be a primary contributing factor in the development of CMD. In addition, plant-based dietary strategies are shown to deter obesity and inhibit inflammation, thereby reducing CMD risk (Swinburn et al., 2004, Greger, 2020). Unfortunately, providing nutritious and affordable foods to Americans is still a challenge (USDA, 2017).

Agricultural research and innovation play an important role in improving the health benefits of the food beyond its conventional nutritional properties and providing sustainable and affordable foods to meet basic caloric and micronutrient needs. The potato is widely recognized as being a superior food choice for both health and nutritional-value-per-dollar when compared to other vegetables. As such, the potato is the most consumed food commodity among Americans. In addition to conventional cultivars, breeding programs have introduced new, specialty cultivars with diverse phytochemical and macro-/micro-nutrient content (Chaparro et al., 2018, Bártová et al., 2015). Extensive in-vitro studies have demonstrated the antioxidant and anti-inflammatory effects of phytochemicals found in several plant-based foods. Human and rodent studies have corroborated these effects. However, despite our basic understanding of the health benefits imparted by potatoes, the bioactivity potential within the vast gene pool of potatoes remains largely unexplored. Specifically, there remains a significant gap in our understanding regarding the effect of bioactive compounds isolated from potatoes or potatoes as a whole food matrices on metabolic pathways and CMD risk factors

In this dissertation, I examined the variation of phytochemical bioactivity within a broad range of potato cultivars and evaluated the potential health outcome of a high phenolic potato diet in a rodent model of obesity. I also investigated the barriers to adopting new specialty cultivars by growers. My hypotheses were: The explorations in this dissertation were conducted through multidisciplinary framework that enabled a holistic evaluation of the phytochemical composition of potato, the potential health benefits, and the barriers for adoption of new cultivars for growers.

First, I compared the in-vitro antioxidant potential of 57 potato cultivars belonging to five different market classes. My research showed that the specialty class (mainly cultivars with purple flesh) contained the highest total phenolic content and the highest AOX capacity in-vitro. Cooking did not change the antioxidant capacity of these phytochemicals. I also evaluated the specific phenolic chlorogenic acid (CGA), which has been shown to deliver several health benefits in vitro, in vivo and in animal models. The highest total CGA content was measured in the Specialty market class. Interestingly, when considering the percentage of total phenolics that could be attributed to CGA content, I observed that some Russet cultivars had high ratio of CGA. This is an important finding as these white-fleshed cultivars represent the primary market class produced and consumed in the United States. Thus, this result demonstrates the potential for development of nutritionally beneficial high CGA cultivars within this accepted market class. These results lay the groundwork for targeted improvement of these cultivars through breeding efforts as well as future research to investigate their ex-vivo or in-vivo bioactivity. For example, future research could explore the interaction of CGA from potato with gut microbiota or their effect on bioavailability and bio-accessibility of macro-nutrients in food. Taken together, my research can be utilized by breeders to drive forward efforts to improve the national value of crops. Furthermore, our results provide consumers (e.g., industry, breeders, and dietitians) with a better understanding of the different potato cultivars and their potential health benefits. Finally, the potato and its byproducts represent a very promising natural colorant for the food industry thanks to its high color intensity and high stability. While my study has focused specifically on phenolic compounds and their bioactivity, additional research is warranted to explore macro-nutrient diversity and bioactivity.

I established an in-vitro system to assess the ACE inhibitory activity of phenolic compounds extracted from cooked potatoes. The ACE inhibition observed was correlated with both CGA and total phenolic content. Specifically, I observed a more than two-fold increase in ACE inhibitory activity with phenolic extracts from purple flesh potatoes compared to a white flesh potato. These preliminary results lay the groundwork for future studies exploring the ACE inhibitory activity across multiple cultivars. Furthermore, the complex content of total small molecule extracts used in our study does not enable characterization of the specific compound(s) responsible for the observed ACE inhibitory activity. While my results suggest that this activity is correlated with phenolic content the extracts also contain non-phenolic small molecules and small peptides. Future studies could investigate the mechanism of ACE inhibition by performing bioassay guided fractionation. Proteins represent another important bioactive compound in potato. While the variation in amino acid profiles of several potato cultivars has been documented, the relationship to bioactivity remains to be investigated and represents an important area of future research.

In the second research project, I evaluated the effect of a high phenolic potato diet (PP) on cardiometabolic health and obesity in a rodent model. Investigations on the health impact of potatoes have traditionally focused on individual constituents, such as proteins, fats, carbohydrates, and micronutrients, or specific phytochemicals despite the fact that our diets are multifaceted and do not consist of one single molecule. Rather food products, which coalesce to form our unique dietary habits, are complex matrices of bioactive compounds and form intricate networks which ultimately influence the bioavailability and bioactivity of each other. For example, we know that macronutrients, like proteins, carbohydrates, and lipids can surround small molecules, more specifically phenols, and modulate their bioavailability and absorption. My research sheds a light on the effect of the phenolic compounds on metabolism when consumed as a part of whole food. In my study, I observed that a diet based on high phenolic potato increased the satiety in leptin-deficient obese mice (ob/ob), resulting in weight loss and reduction in adiposity. The obese mice on the purple potato diet lost weight when compared to the obese with the control (non-potato) diet. The same trend was observed in the lean animal model (+/ob) who consumed the purple potato diet for 10 weeks. As a consequence of eating less, adiposity was reduced in both obese and lean animals. This is an important observation as previous clinical studies have revealed that phenolic compounds can induce satiety. Furthermore, resistant starch, protease inhibitors are other components of potato that could have played a role in this phenomenon. These observations were corroborated by a non-targeted metabolomics study of serum and liver in obese and lean animals, who had potato diet or control. The segregation of metabolite fingerprints in liver and serum of animals on the potato diet compared to the controls suggests a strong diet induced host metabolic shift. The reduction of cholesterol in the serum, along with reduction of triacylglycerol metabolites in the liver, among the obese animal who had potatoes compared to obese who were on a control diet, are the indicators of the effect of potato on modulating lipid metabolism. This research had some limitations, as such limitations arise from method. The diet I used was high phenolic potato diet compared to control diet, which was the

HAMS, the study did not have a low phenolic potato control. More research needs to investigate the effect of other components of potato as they could have played role in these observations. For example, the change in gut microbiota after a high phenolic potato diet needs to be compared to a low phenolic diet. In addition to phenolics, the varieties with different resistant starch, fiber, and protease inhibitors also need to be evaluated in regard to changing the microbiome composition. In a high phenolic diet, the bioavailability and broadcastability of phenolics are important leading to the need to be studied more in detail. As such the breeders can focus on increasing the specific phytochemicals that are more accessible and active in the body, for the new cultivars.

Agricultural research and innovation play an important role in improving the health benefits of the food beyond its conventional nutritional properties. Despite this variation the potato supply chain has mainly relied on one market class and one cultivar: the white and russet. As a result, consumers are missing access to variants that contain beneficial macro-and micronutrients and phytochemicals. In my last study, I sought to understand the decision-making process of potato growers related to the adoption of new cultivars. Each year, growers must decide which cultivar to grow, and therefore this decision has an impact on the availability of a cultivar to consumers. This decision can be considered vital to public health as these cultivars are demonstrated to vary in traits important to human health. Adopting a new approach (either using new technology or adopting a new crop) brings risk to the system and is therefore associated with complex psychological and economic factors. I developed a multi-factorial model to explain adoption in a potato growing system. An integration of Theory of Planned Behavior, Rational Expectation Hypothesis, and Diffusion of Innovation models identify economic and social factors that influence grower decision making. Growers that were more aware of specialty cultivar innovation and associated consumer demand were more open to SCs adoption. Other influencing factors include a grower's experience selling a specialty cultivar in the previous year and access to diverse markets. Based on these data, a new model was developed to explain the grower decision-making processes in adopting specialty cultivars. The model demonstrates that the current barriers to adoption are access to the primary buyers such as warehouses, retailers, and households. Taken together, my research demonstrates how rational expectations stem from economic outcomes, knowledge, and experience in the potato industry. These results are important in helping to consider opportunities for growers to access new, higher-value markets, which may also improve consumer access to nutritious cultivars.

Further research needs to be done to understand different sectors of the Agri-food system surrounding specialty cultivars and their markets. Potato stakeholders, their concerns, and the need to develop a new market channel for the specialty cultivars need to be dug into. Another aspect of successful innovation is adoption among the population. Research needs to be done to evaluate the market and consumers' readiness to accept new potato cultivars.

While my research generated important preliminary findings related to the phenolic content and bioactivity of potato cultivars and their potential health benefits, it has also generated more questions to be addressed in future research. The core message of this dissertation is that the variation in the potato gene pool can be leveraged through breeding to improve the nutritional value of this most consumable crop. The vast gene pool of potatoes provides a golden opportunity to breed a golden variety with higher health benefits. My dissertation highlights the fact that there is a link between a diet high in phytochemicals and reduction of obesity and consequence cardiometabolic disorders. Next steps will require understanding what part of the potato is driving this improvement, and what are the main targets for these molecules in the body. Finally, we have also demonstrated that while there are barriers to grower adoption, growers do indicate that these new cultivars are compatible with their farming operation and can be sold with higher profits. Thus, there is potential for a new markets targeting new improved health promoting potato cultivars.