

Phytochemical Variation: An Argument for Intentional Cultivation
of Plants Grown for their Bioactive Compounds

Introduction

Secondary metabolites are compounds formed within an organism that are not directly involved in the essential functions of growth, development, and reproduction. Instead, secondary metabolites in plants (and other organisms) are deployed in functions that increase fitness for survival: such as—but not limited to—plant-microbe interactions, pheromones, and defenses against predation (Chadwick and Whelan 2008). There are still millions of mysteries that surround these specialized compounds, but we have been able to infer some of their uses and impacts in the environment and, when consumed, in the human body (Jain et al. 2019).

One of the major human uses of phytochemicals beyond basic nutrition is in pharmaceuticals, where plants containing certain compounds or compounds isolated from those plants are employed as medicine (Jain et al. 2019). Phytochemical medicines are based in historical medicine practices like Ayurveda and Traditional Chinese Medicine in combination with modern scientific analyses of secondary metabolites and their biological activities; scientific analysis of these compounds has in some cases demystified the mechanisms of certain traditional plant medicines and their efficacy. The vast diversity of secondary metabolites produced by plants implies an equally vast number of uses in medicine. Some types of previously studied secondary metabolites include phenols, alkaloids, sterols, tannins, saponins, and flavonoids (Gokhale and Wadhwani 2015). For example, *Arbutus unedo*—a folk medicine plant historically used in the Mediterranean as an antiseptic, diuretic, laxative, and astringent (Morgado et al. 2018)—extract was analyzed for antimicrobial activity against several bacterial strains known for their resistance to many antibiotics, and it was found to have an antagonistic impact on *E. coli* and *S. aureus* (Dib et al. 2011).

Despite the effectiveness of many phytochemical compounds in pharmacology, they can be limited by their accumulation in a utilized plant specimen. Genetics, growth conditions, and post-harvest processing especially have a wide range of effects on the levels of secondary metabolites present in a particular specimen (Verma 2015). Because of the wide availability of studies on the nutritional impacts of processing, this review will focus on the genetic and environmental sources of chemical variation; how they might benefit or disable the associated compounds; and ways that knowledge might be applied in the production of phytopharmaceuticals.

Genetically-Induced Alterations

The genetics of a species or variety have been repeatedly noticed as a major significant factor determining the phytochemical composition of any given plant specimen (Cirak and Radusiene 2019; Kanellis and Manganaris 2014; Li, Tsao, and Deng 2012)--though others have found conflicting evidence where additional factors created the greatest variation (Aherne et al 2009). In a study of carotenoids, compounds that show up as pigments in plants and that have antioxidant capabilities in the human body, in twenty tomato varieties grown in the same location, scientists found statistically significant differences in accumulation in three varieties; there was in some cases more than double the amount of carotenoids in the top two analyzed varieties than in any other (Li et al. 2012). In *Hypericum* species, the greatest chemodiversity has been found between genotypes, while various accessions of the same genotype have little variability based on where and when they are grown or harvested (Cirak and Radusiene 2019). Significant differences in phytochemical contents among *Capiscum annuum* varieties have also been documented (Hervert-Hernández 2010).

From 1950-1999, as popular crop plants were bred and selected for larger yields, the average nutritional content decreased in proteins, calcium, phosphorus, iron, riboflavin, and ascorbic acid (Davis et al. 2004). All these compounds carry out essential metabolic functions in the human body, and majorly decreasing our intake of them can negatively impact nearly all

organ systems in some manner (Iqbal 2004; Powers 2003). Similarly, a loss of primary and secondary metabolites in cultivated plants should minimize their efficacy as medicines. This exposes the importance of analyzing crop plants for phytochemical content and genotype and taking these measurements into consideration when breeding or growing plants for human consumption. Breeding plants specifically for yield, rather than with a holistic perspective that incorporates genetic diversity and phytochemical content, could continue to produce exponentially nutrient-weak crops that have little value in subsistence and medicine. Conversely, taking care to preserve genotypic variation would benefit our understanding and our uses of these plants and the nutrients they contain.

Cultivation-Induced Alterations

Cultivation conditions and what a plant experiences as it grows exert another major influence on phytochemical contents. Secondary metabolites are often produced for the sake of self-regulation (hormones), defense, and communication with others of the same species (pheromones) or with individuals of another species (allomones). So, specific conditions—such as droughts, competition with other species, varied soil compositions, or predation by herbivores or insects—can trigger the development or suppression of these compounds (Macías et al. 2007). In cases where a specific compound has been identified as the agent of a phytopharmaceutical, incorporating the triggering condition can create a larger store of the targeted chemical. In a 2003 study, Poulev et al. used acetate, methyl salicylate, methyl jasmonate, and chitosan to elicit bioactive compounds in 966 plant species and found a significant and reproducible doubling of species with noticeable pharmacological bioactivity.

Some defensive secondary metabolites are created or accumulated in response to tissue damage, like phytoalexins which are antibiotics synthesized in response to pathogenic attack; allelopathic compounds are constantly created to defend the plant or even secreted into the soil and cause damage to other species, but they can be amplified in response to tissue damage (Macías et al. 2007). These chemicals are not only useful in protecting the plant. The

phytoalexin resveratrol found in tea, wine, cereals, fruits, and vegetables is known to lower glucose levels in type-1 and type-2 diabetes and to work against related health complications, among many other bioactive functions (Sindhu et al 2020). Phytoalexin content can be increased in some plants as much as two or three times the usual amount when the plants are inoculated with pathogens (Poulev et al 2003). However, these mechanisms can be altered during the process of plant breeding if proper care and measurements are not taken (Davis et al 2004). Promoting the formation and observation of these compounds may reveal their ability to protect important crop plants in the field and to support the human body when ingested.

Location-related factors—like soil content, climate, sun or shade exposure, and precipitation—are the other major cultivation aspects that impact phytochemical concentrations. In *Withania somnifera*, one of the most important Ayurvedic cognitive medicine plants, drought stress induces not only morphological alterations but also an increase in carotenoid, anthocyanin, flavonoid, proline, and starch content (Kannan and Kulandaivelu 2011). *Zea mays*, an essential food crop, is known to increase benzoxazinoid content in aboveground tissues and terpenoid phytoalexins in belowground tissues under drought conditions (Vaughan 2018). Cold temperatures can decrease carotenoids and flavonoids and increase phenolic acids, glucosinolates, and proline in *Brassica oleracea var. acephala* (Šamec et al 2022). Whereas in *Agastache rugosa*, maintaining root temperatures at 28°C creates the greatest accumulation of two major bioactive compounds, rosmarinic acid and tilianin (Lam et al. 2020). Low temperatures, drought, salinity, and increased UV-B radiation are all sources of oxidative stress that cause some plants to increase their production of antioxidant compounds (Cirak and Radusiene 2019). Improving antioxidant content for the sake of their medicinal actions and health benefits could be intentionally induced by growers by introducing one of these stressors in a capacity that stimulates secondary metabolite production with minimal effect on plant morphology or taste.

Plants respond also to their growing medium. However, soils vary greatly in composition with their location. This variation is imprinted upon the plant's morphological or phytochemical structures (Cirak and Radusiene 2019). *Cloeus amboinicus*, a perennial herb rich in rosmarinic acid, flavonoids, and abietane diterpenoids, grown in Poland produced plants significantly lower in protein and terpenoid content but higher in polyphenols, as opposed to its native soils in Indonesia (Ślusarczyk et al. 2021). The conflicting study mentioned in the previous section reported a greater variation in tomato carotenoid content and bioavailability by growing location than by genetic variety (Aherne et al. 2019).

Discussion

Each plant, based on its genotype, has a unique reaction to environmental conditions. It is therefore essential to understand the sources of these reactions and their chemical impact. With this information, growers can induce accumulation of desired secondary metabolites or avoid conditions and genotypes that reduce these helpful chemicals. A great amount of experimentation is still required to suss out the variety of secondary metabolites that exist, their bioactivity in the human body, and the best conditions for and genotypes of specific species with the most amenable phytochemical contents.

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