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Therapeutic Potential of Bioactive Compounds of Prunus Laurocerasus in the Management of Metabolic Syndrome

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Abstract: *Background:* Obesity and overweight are major global health concerns and it is obvious, that the trend of the cases is growing over time. These states are closely linked to type 2 diabetes mellitus, cardiovascular disease, hypertension, heart failure with preserved ejection fraction and various malignancies. Excess adiposity promotes insulin resistance, chronic inflammation, dyslipidemia, endothelial dysfunction, and neurohormonal activation. Growing interest in natural product–based therapeutics has highlighted polyphenol-rich plant extracts as potential adjunctive strategies for metabolic regulation. Cherry laurel (*Prunus laurocerasus*) is a polyphenol-rich fruit containing bioactive compounds such as quercetin, kaempferol, chlorogenic acid, and anthocyanins with reported anti-obesity effects. *Methods:* Extracts of fresh, frozen, and dried *Prunus laurocerasus* fruits, collected from different regions of Georgia were analyzed for polyphenolic content. The biological activities of the identified bioactive compounds were contextualized based on previously published preclinical studies evaluating their effects on adipogenesis, lipid metabolism, glucose homeostasis, inflammatory signaling and energy regulation. *Results:* All extracts demonstrated consistently high polyphenolic content regardless of processing method or geographic origin. Chlorogenic acid and anthocyanins were identified as the predominant constituents, followed by substantial levels of quercetin and comparatively lower concentrations of kaempferol. *Conclusion:* The polyphenolic profile of *Prunus laurocerasus* suggests its potential as a multifaceted adjunctive strategy in metabolic syndrome management, warranting further translational and clinical investigation.

Keywords: *Prunus laurocerasus*, Metabolic syndrome, Anthocyanins, Chlorogenic acid, Valorization

Introduction

Obesity and overweight currently represent the most significant challenges in global clinical management, with a well-established association between excess adiposity and the rising incidence of type 2 diabetes mellitus (T2D), cardiovascular disease (CVD), and several forms of cancer. These conditions collectively impose a substantial burden on healthcare systems, remaining leading causes of morbidity and mortality worldwide. Since

1990, childhood and adolescent obesity has increased more than fourfold globally, and in most nations, the prevalence of obesity now exceeds that of being overweight. Currently, approximately 1.4 billion adults are classified as obese, and projections indicate that these trends will continue to escalate by an estimated 30% over the next decade (Chew et al., 2023; O'Neill & O'Driscoll, 2015).

The pathophysiology of obesity is characterized by complex systemic disruptions. Excess adiposity serves as a major independent risk factor for arterial hypertension by increasing sympathetic nervous system activity, activating the renin–angiotensin–aldosterone system (RAAS), and promoting sodium retention (Hall et al., 2015). Furthermore, visceral fat acts as an active endocrine organ, secreting adipokines and inflammatory mediators like TNF-α and IL-6. these cytokines impair endothelial function, increase vascular resistance, and accelerate atherosclerosis by inducing dyslipidemia and chronic inflammation. Consequently, the resulting increase in cardiac workload leads to structural changes such as left ventricular hypertrophy and diastolic dysfunction, often progressing to heart failure with preserved ejection fraction (HFpEF) due to myocardial fibrosis (Seravalle et al., 2017, Lavie et al., 2009, Ridker et al., 2000, Kenchaiah et al., 2002, Packer 2018)

Beyond cardiovascular complications, obesity is the strongest modifiable risk factor for type 2 diabetes (T2D) (Kahn et al., 2006). The expansion of adipose tissue leads to increased free fatty acid release and ectopic lipid accumulation, which triggers chronic inflammation and impairs insulin signaling in skeletal muscle, adipose tissue and the liver (Samuel et al., 2016). Visceral obesity is particularly detrimental, as it is closely associated with β-cell dysfunction and the progression from insulin resistance to overt diabetes (Eckel et al., 2011). Additionally, obesity significantly worsens the prognosis for several malignancies, including colorectal, pancreatic, and postmenopausal breast cancers, leading to higher cancer-related mortality rates (Lauby-Secretain et al., 2016, Calle et al., 2003).

While traditional management approaches, including lifestyle modification and pharmacotherapy, exist, they often provide limited long-term success, and obesity-related mortality remains stubbornly unchanged. This gap in clinical efficacy has fueled growing interest in naturally derived bioactive compounds as complementary strategies. Flavonoids, including quercetin, total phenols, anthocyanins, and kaempferol, offer promising therapeutic potential by targeting inflammatory pathways, enhancing insulin sensitivity, and improving lipid profiles **(**Godyla-Jabłoński et al., 2024; Oumeddour et al., 2024; Rubio-Ruiz et al., 2019).

In light of this increasing interest in natural product–based therapeutics, the present study investigates the potential benefits of cherry laurel (*Prunus laurocerasus*) bioactive compounds. To address the challenge of seasonal availability, we examined the juice of fresh and frozen fruit, dried products, and processing residues (skin and pomase-waste) from various locations across Georgia. Notably, this research highlights the additional benefit of waste valorization; by demonstrating that processing by-products retain significant bioactive potency, this study supports sustainable strategies for the development of high-value nutraceuticals from agricultural side-streams Previous studies confirm the rich phytochemical profile and antioxidant potential of Prunus laurocerasus extracts (Altuntaş et al., 2018; Konuk et al., 2024; Margalitadze et al., 2025).

While the complexity of metabolic syndrome suggests that dietary interventions are most effective when paired with comprehensive lifestyle changes, preclinical evidence underscores the potent role of specific flavonoids namely quercetin, chlorogenic acid, kaempferol and anthocyanins in improving metabolic health. These compounds exert overlapping anti-inflammatory, antioxidant, and metabolic-regulatory actions through a sophisticated network of molecular signaling (Godyla-Jabłoński et al., 2024; Oumeddour et al., 2024).

As a primary constituent identified in Georgian wild *Prunus laurocerasus* extracts, chlorogenic acid (CGA) plays a pivotal role in the systemic management of metabolic syndrome. CGA primarily targets lipid metabolism by activating the AMPK (adenosine monophosphate-activated protein kinase) pathway. Which leads to increased phosphorylation of acetyl-CoA carboxylase (ACC) to serve a dual purpose: suppression of the *de novo* synthesis of fatty acids and simultaneously promotes lipid oxidation **(**Oumeddour et al., 2024; Godyla-Jabłoński et al., 2024).

Our focus on CGA is further justified by its impact on hepatic health. In hepatocyte models, CGA has been shown to significantly reduce triglyceride accumulation by downregulating key lipogenic regulators, specifically SREBP-1c and fatty acid synthase (FAS). Beyond its independent effects, CGA offers a strategic clinical advantage; evidence suggests it may enhance metabolic signaling when combined with conventional treatments like metformin, resulting in a more potent, synergistic anti-lipogenic effect **(**Rubio-Ruiz et al., 2019**).** This interaction positions the CGA-rich profile of cherry laurel as a high-value candidate for adjunctive therapy in patients struggling with insulin resistance and non-alcoholic fatty liver disease (NAFLD).

Anthocyanins, including cyanidin-3-O-glucoside, further complement these actions through diverse metabolic and endothelial-protective pathways (Oumeddour et al., 2024). These pigments exert anti-atherosclerotic, antihypertensive, and antioxidant effects that support the maintenance of body weight and improved lipid profiles. At the molecular level, anthocyanins decrease lipogenesis while simultaneously increasing fatty acid oxidation by activating the AMPK pathway and stimulating mitochondrial biogenesis. They also modulate PI3K–Akt and GLUT1/4 signaling to enhance insulin sensitivity, inhibit NF-κB to reduce systemic inflammation, and promote a favorable M1 to M2 macrophage polarization **(**Godyla-Jabłoński et al., 2024; Oumeddour et al., 2024**)**. Furthermore, experimental studies demonstrate that anthocyanins improve metabolic syndrome through gut microbiota modulation and increased short-chain fatty acid production **(**Du et al., 2025).

Quercetin, in particular, has demonstrated the ability to significantly improve adiposity, dyslipidemia, and glucose intolerance. In rodent models, it produces coordinated transcriptomic changes in hepatic and adipose tissues, directly enhancing insulin sensitivity. Its systemic impact includes the reduction of epididymal and retroperitoneal fat, lower serum and hepatic triglycerides, and improved fasting insulin levels **(**Kabelova et al., 2022**)**. Beyond these direct metabolic effects, quercetin also improves antioxidant defenses and reduces hepatic steatosis (Rubio-Ruiz et al., 2019).

Similarly, kaempferol contributes to body weight reduction and improved glycemic parameters primarily by targeting the central nervous system. By suppressing hypothalamic inflammation and altering central energy balance signaling, kaempferol decreases microglial activation in the arcuate nucleus. This central administration leads to marked weight loss, reduced feed efficiency and improved metabolic outcomes (Romero-Juarez et al., 2021).

A critical emerging theme across all compounds is their ability to reshape the gut microbiota and stimulate the production of short-chain fatty acids (SCFAs). For instance, anthocyanin-mediated benefits in high-fat diet models have been linked to the proliferation and increased acetic acid production (Du et al., 2025). These protective phenotypes are so robust that they have proven transferable via fecal microbiota transplantation. Collectively, these flavonoids act as multi-target agents that bridge the gap between gut health, central energy regulation, and peripheral metabolic function, offering a comprehensive pharmacological basis for their use in metabolic syndrome management.

While each flavonoid exhibits unique primary targets—such as quercetin's focus on hepatic transcriptomic shifts, kaempferol's regulation of hypothalamic microglial activation, and anthocyanins' robust activation of mitochondrial biogenesis—they converge on a unified therapeutic front. By collectively modulating the AMPK/PI3K–Akt signaling axes, suppressing NF-κB-mediated inflammation, and reshaping the gut microbiota to favor short-chain fatty acid production, these compounds offer a sophisticated, multi-level defense against metabolic dysfunction **(**Godyla-Jabłoński et al., 2024; Oumeddour et al., 2024; Du et al., 2025**).** This integrated mechanism suggests that a combination of these bioactives, as found naturally in *Prunus laurocerasus*, may provide a more comprehensive intervention than any single isolated compound.

In this context, increasing attention has been directed toward plant-derived sources rich in bioactive compounds **(**Altuntaş et al., 2018**).** *Prunus laurocerasus* L. (cherry laurel) represents a promising candidate due to its high polyphenolic content and documented biological activities (Kaya Kartal et al. 2025, Konuk et al. 2024) . The fruit contains significant amounts of flavonoids and various anthocyanins, which are known to exert antioxidant and anti-inflammatory effects (Cai et al., 2004; Djeridane et al., 2006; AbdelRahim and El-Beltagi, 2019**)**. When compared with international datasets (Table 1.) (Halilova et al., 2010; Kaya Kartal et al., 2025; Konuk et al., 2024; Todorova et al., 2025**)**, Our findings suggest that Georgian wild cherry laurel demonstrates strong competitiveness in bioactive compound content.

Aim and Methods

In light of the increasing interest in natural product–based therapeutics, we aimed to investigate the potential benefits of Georgian autochthonus wild cherry laurel (*Prunus laurocerasus*), collected from different locations of western Georgia, in particular, Erge (41°33'41.0"N, 41°41'48.0"E) and Tkhilnari (41°33'49.0"N, 41°39'11.0"E), bioactive compounds in the management of these conditions. We studied the juice of fresh and frozen fruit, the dried product, and, as an additional strategic benefit, the processing residues (skin and pomase). The inclusion of these residues highlights an opportunity for waste valorization; our data reveals that these by-products are not merely industrial waste but are potent carriers of secondary metabolites. This evaluation of

primary fruit products and their processing by-products highlights a sustainable and economically optimized model for pharmaceutical applications.

Regardless of storing, processing method or geographic origin, wild cherry laurel fruit extracts demonstrated a consistently high polyphenolic content, a naturally occurring flavanols with well-documented antioxidant and anti-inflammatory properties that have attracted increasing interest in metabolic disease research. Prior to chemical analysis, we blanched our samples with 80% hot ethanol and then processed it for farther chemical analysis.

Quantitative Determination of Flavonoids

The total flavonoid content was determined using the $AlCl_3$ spectrophotometric method. One milliliter of the extract was mixed with 5 mL of distilled water and 0.3 mL of 5% $NaNO_2$, followed by incubation for 5 minutes. Subsequently, 0.3 mL of 10% $AlCl_3$ was added, and the mixture was incubated for an additional 6 minutes. Afterward, 2 mL of 1 N NaOH was added. The absorbance of the resulting solution was measured at 510 nm. The results were expressed as milligrams of quercetin equivalents per gram of sample (mg QE/g), using the calibration curve: $y = 1.154\ x - 0.002$ ($R^2 = 0.999$). (Datuashvili et al., 2025, Abashidze et al., 2024)

Quantitative Determination of Total Anthocyanins

The total anthocyanin content was determined using a rapid direct UV–Vis spectrophotometric method at a wavelength of 520 nm. Sample extraction was performed using 70% ethanol containing 0.1% HCl. The absorbance of the analytical extract was measured at 520 nm (A_{520}) and 700 nm (A_{700}). The corrected absorbance was calculated using the following equation: $A\_corr = A_{520} - A_{700}$ The extraction solvent (70% EtOH + 0.1% HCl) was used as a blank. The anthocyanin concentration was calculated based on the Beer–Lambert law: $c\ (mol/L) = A\_corr / (\varepsilon \times b)$ where $\varepsilon = 26{,}900\ L \cdot mol^{-1} \cdot cm^{-1}$ and $b = 1$ cm. The concentration in mg/L was calculated as: $C\ (mg/L) = (A\_corr \times MW) / (\varepsilon \times b) \times 1000$ where MW (malvidin-3-O-glucoside chloride) = 528.9 g/mol. The results were expressed as milligrams of malvidin-3-O-glucoside equivalents per gram of sample (mg/g) (Giusti et al., 2001)

Determination of Antioxidant Activity by 50% Inhibition of 0.1 mM DPPH Radical (IC_{50})

Antioxidant activity was evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging spectrophotometric assay. Appropriately diluted extracts at different concentrations were mixed with DPPH solution. Specifically, a 1.0 mL aliquot of each extract was combined with 3.0 mL of 0.1 mM DPPH methanolic solution. The reaction mixture was incubated in the dark at room temperature for 30 minutes, after which the decrease in absorbance was measured at 517 nm using a UV–Vis spectrophotometer. The radical scavenging activity was expressed as the percentage of DPPH inhibition (In%), calculated using the following equation:

$$In\% = [(Ac - As) / Ac] \times 100$$

where Ac is the absorbance of the 0.1 mM DPPH ethanolic solution (control), and As is the absorbance of the reaction mixture containing the sample extract. The extract concentration required to achieve 50% inhibition of the DPPH radical (IC_{50}) was calculated using the following equation:

$$IC_{50} = (m \times V \times F \times 100) / In\%_{50}$$

where *m* is the mass of the tested sample (mg), *V* is the volume of the sample extract (mL), *F* is the dilution factor, and $In\%_{50}$ represents the percentage of DPPH inhibition within the 45–55% range used to interpolate the IC_{50} value. The results were expressed as milligrams of sample required to inhibit 50% of the DPPH radical (mg IC_{50}). (Brand-Williams et al., 1995)

Determination of Total Phenolic Content

Total phenolic content was quantified using the Folin–Ciocalteu colorimetric assay. Briefly, 1 mL of the extract was mixed with 1 mL of Folin–Ciocalteu reagent. After a 3-minute reaction period, 1 mL of 10% Na_2CO_3 was

added, and the mixture was diluted to a final volume of 10 mL with distilled water. The reaction mixture was allowed to stand for 90 minutes at room temperature, after which absorbance was measured at 750 nm. The results were expressed as milligrams of chlorogenic acid equivalents per gram of sample (mg/g). (Datuashvili et al., 2024)

Determination of Total Phenolic Acids

Total phenolic acids were determined spectrophotometrically at 320 nm. In brief, 250 µL of the extract was combined with 250 µL of 0.1% ethanolic HCl and 4.55 mL of 2% HCl to reach a final volume of 5.05 mL. The mixture was vortexed thoroughly and incubated at room temperature for 15 minutes. Absorbance was then recorded at 320 nm against an appropriate reagent blank. Quantification was performed using a calibration curve, and the results were expressed as milligrams of caffeic acid equivalents per gram of sample (mg/g) (Abashidze et al., 2024)

Results and Discussion

Our analytical results revealed that while Georgian autochthonous Prunus laurocerasus (both wild and cultivated) contains a diverse polyphenolic profile (Margalitadze et al., 2024), the concentrations of individual compounds varied significantly among the wild fruit fractions. Chlorogenic acid and anthocyanins were found as the predominant, followed by substantial levels of quercetin. In contrast, kaempferol was identified in comparatively minor concentrations across all samples, regardless of their geographic origin in Georgia. Given this distribution, our investigation into metabolic signaling and therapeutic potential focuses primarily on the dominant bioactive drivers—chlorogenic acid, anthocyanins, and quercetin—which represent the most significant pharmacological components of the our samples of wild cherry laurel extracts. A critical finding of this study is the distribution of these metabolites across the fruit's physical components.

The highest concentrations of bioactive compounds were consistently determined in the pulp, followed by the juice, with the lowest concentrations detected in the processing residues (waste). Specifically, the pulp contained 49.61 mg/g of total phenols and 37.99 mg/g of total flavonoids, nearly doubling the concentrations found in the juice.The same correlation was observed regarding antioxidant activity. The pulp exhibited the most potent radical scavenging capacity (lowest IC_{50}), while the waste fraction showed the lowest activity. However, despite exhibiting lower concentrations relative to the pulp and juice, the wild cherry laurel processing residues still retain appreciable levels of phytochemicals, including 15.75 mg/g of total phenols and 10.24 mg/g of total flavonoids (Chart 1,2,3,4) From a sustainability perspective, these findings underscore the potential of such by-products to function as economically viable raw materials. The retention of significant secondary metabolites in agricultural side-streams supports a circular economy model, allowing for the subsequent extraction and utilization of these compounds in the functional food and pharmaceutical sectors.

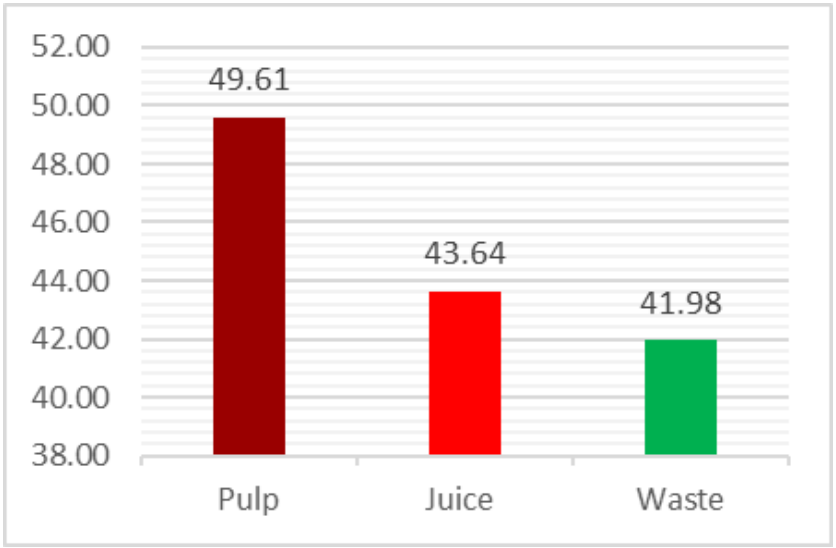

Figure 1. Total phenols of wild cherry laurel (mg/g, as chlorogenic acid equivalents)

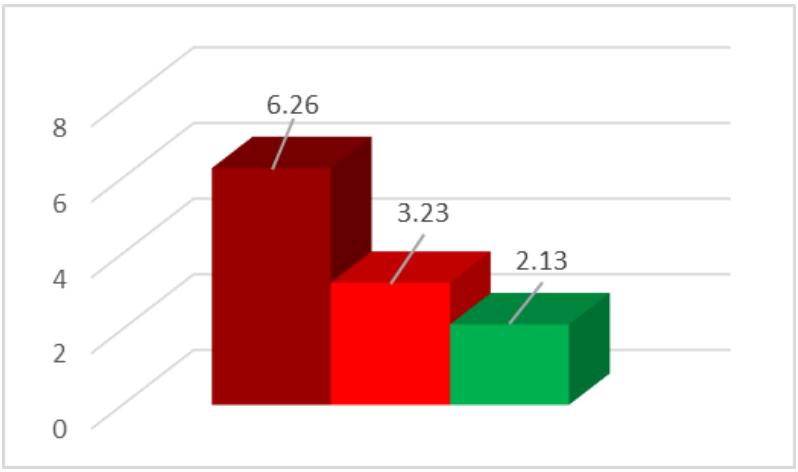

Figure 2. Total anthocyanins of wild cherry laurel (mg/g)

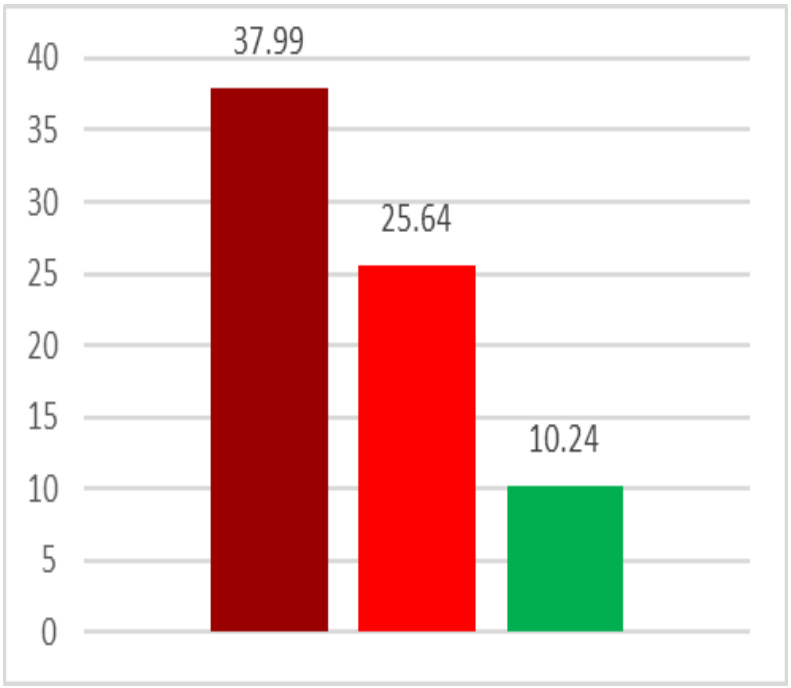

Figure 3. Total flavonoids of wild cherry laurel (mg/g, as quercetin equivalents)

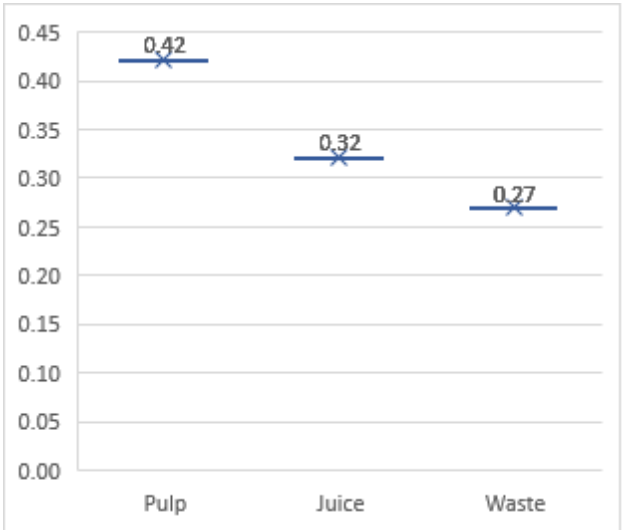

Figure 4. Antioxidant activity (0,1 mM DPPH, IC_{50} mg of sample)

Table 1. Comparative analysis of bioactive compound levels in Georgian wild cherry laurel versus international literature values

Compound	Georgian wild cherry laurel pulp	International (Avg. numbers from literature)
Total Phenols	49.61 mg/g	15.0 – 40.0 mg/g (DW)
Anthocyanins	6.26 mg/g	0.5 – 2.5 mg/g
Flavonoids	37.99 mg/g	1.0 – 15.0 mg/g

Conclusion

The present study demonstrates that Georgian autochthonous wild cherry laurel (*Prunus laurocerasus*) represents an exceptionally rich and consistent source of bioactive secondary metabolites, specifically chlorogenic acid, anthocyanins, and quercetin. Notably, this phytochemical profile remains stable regardless of the geographic origin within Georgia or the storage method, suggesting the plant's reliability as a high-quality raw material for future therapeutic applications. This unique composition provides a potent "natural cocktail" for multi-target metabolic defense. By collectively modulating critical pathways such as AMPK and PI3K–Akt signaling, and suppressing NF-κB-mediated inflammation, these compounds offer a sophisticated defense against the core pathologies of metabolic syndrome. Our findings suggest that *P. laurocerasus* extracts can provide essential protection against systemic oxidative stress and serve as a valuable adjunctive strategy alongside standard clinical treatments for obesity, insulin resistance, and type 2 diabetes. Furthermore, while the fruit pulp and juice serve as the primary reservoirs for these metabolites, our data reveals that processing residues (waste) retain significant bioactive potency. These residues represent a high-value source for nutraceutical development. By successfully valorizing these agricultural side-streams, this research supports a sustainable circular economy model that reduces environmental impact while providing cost-effective medicinal resources. Collectively, these findings establish a rigorous foundation for the development of specific Georgian-sourced functional foods and pharmaceutical additives aimed at addressing the escalating global epidemic of obesity and metabolic dysfunction.

Scientific Ethics Declaration

* The authors declare that the scientific ethical and legal responsibility of this article published in EPSTEM journal belongs to the authors.

Conflict of Interest

* The authors declare that they have no conflicts of interest.

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