

Phytochemical Characterization and In Vitro Antidiabetic Activity of *Aruncus dioicus* from Vietnam

Thuc Bui Thi¹, Tung Nguyen Van Duy²

¹ Vietnam Academy of Science and Technology

Email: buithithuc24@gmail.com

² Michigan State University, USA

Email: nguy1640@msu.edu

Abstract: *This study presents a phytochemical and pharmacological investigation of Aruncus dioicus, a medicinal plant collected from the northeastern coastal region of Vietnam. In light of the growing global prevalence of type 2 diabetes mellitus (T2DM), the search for natural compounds capable of modulating key enzymes involved in glucose metabolism, particularly Protein Tyrosine Phosphatase 1B (PTP1B) and α -glucosidase, remains an important research objective. The experimental methods employed included: botanical identification, extraction, chromatographic separation, and biological activity evaluation. As a result, eleven pure compounds were isolated. Structural determination via ¹H- and ¹³C-NMR spectroscopy revealed these constituents as phenylpropanoids, phenolic acids, nucleosides, and ester derivatives, thereby establishing a distinctive chemical profile for the Vietnamese population of A. dioicus. In vitro enzyme inhibition tests demonstrated significant biological activity. p-coumaric acid (Compound 3) and cinnamic acid (Compound 4) exhibited effects on PTP1B, with IC₅₀ values of 0.25 μ M and 1.16 μ M, respectively, higher than the activity of the reference compound ursolic acid (IC₅₀ = 3.5 μ M). Furthermore, ethylparaben (Compound 7) and cinnamic acid exhibited α -glucosidase inhibition, with potencies approximately five- to six-fold greater than that of acarbose. These findings suggest that A. dioicus is a potentially valuable source of antidiabetic agents and emphasize the significance of phenylpropanoid derivatives in enzyme inhibition associated with glucose metabolism, thereby providing a scientific foundation for subsequent pharmacological investigations.*

Keywords: *Aruncus dioicus; phenylpropanoids; PTP1B; α -glucosidase; antidiabetic activity.*

1. Introduction

Type 2 diabetes mellitus (T2DM) constitutes a persistent global health challenge, distinguished by chronic hyperglycemia resulting from peripheral insulin resistance and progressive pancreatic β -cell dysfunction. According to the American Diabetes Association, T2DM accounts for approximately 90–95% of all diabetes cases worldwide and represents a rapidly growing burden on global healthcare systems, particularly in developing countries such as Vietnam (American Diabetes Association, 2026).

Although current pharmacological therapies are clinically effective, they are frequently associated with notable limitations. For instance, α -glucosidase inhibitors, including acarbose, are commonly linked to gastrointestinal adverse effects such as flatulence and diarrhea, while thiazolidinediones have been reported to induce weight gain and fluid retention. These drawbacks have prompted increasing interest in the discovery of bioactive natural products capable of modulating multiple metabolic targets with reduced side-effect profiles (Tundis et al., 2010; Hanhineva et al., 2010).

This study focuses on two key enzymes that play critical roles in glucose homeostasis: α -glucosidase (EC 3.2.1.20) and protein tyrosine phosphatase 1B (PTP1B). α -Glucosidase is a membrane-bound enzyme localized at the brush border of the small intestine, where it catalyzes the final step of carbohydrate digestion by hydrolyzing disaccharides and starch into absorbable glucose. Excessive α -glucosidase activity results in rapid postprandial hyperglycemia, which significantly increases cardiovascular risk in patients with diabetes (Lebovitz, 1997; Kashtoh & Baek, 2022). Inhibition of this enzyme delays carbohydrate digestion by competitively blocking access of dietary carbohydrates to the active site, thereby reducing postprandial glucose excursions. Numerous studies have demonstrated that plant-derived phenolic compounds and flavonoids can selectively inhibit α -glucosidase, highlighting their therapeutic potential as natural antidiabetic agents (Tundis et al., 2010).

PTP1B is a non-receptor protein tyrosine phosphatase that functions as a key negative regulator of insulin signaling. Upon insulin binding, the insulin receptor undergoes autophosphorylation, triggering a downstream signaling cascade involving insulin receptor substrate 1 (IRS-1) and the PI3K/Akt pathway, ultimately promoting glucose uptake through GLUT4 translocation. PTP1B attenuates this signaling by dephosphorylating both the insulin receptor and IRS-1, thereby terminating insulin signal transduction (Goldstein, 2001; Sun et al., 2016). Elevated PTP1B expression and activity have been consistently observed in obesity and T2DM and are strongly associated with insulin resistance. Conversely, PTP1B-deficient animal models exhibit enhanced insulin sensitivity and resistance to diet-induced obesity, underscoring its therapeutic relevance (Zabolotny et al., 2002). Despite extensive efforts, the development of synthetic PTP1B inhibitors has been hindered by challenges related to selectivity—particularly against the closely

related T-cell protein tyrosine phosphatase (TCPTP)—as well as poor cellular permeability. In this context, naturally occurring small molecules represent promising alternatives for selective PTP1B inhibition (Zhang & Zhang, 2007; Liu et al., 2022).

Aruncus dioicus (Walter) Fernald, commonly known as Goat's Beard and formerly classified as *Aruncus sylvestris*, is a perennial plant belonging to the Rosaceae family and distributed throughout temperate and subtropical regions of the Northern Hemisphere. In Vietnam, this species grows naturally in high-altitude mountainous areas and on limestone islands, particularly in Quang Ninh Province. In traditional East Asian and European medicine, *A. dioicus* has been used for the treatment of hemorrhage, detoxification, tonsillitis, and fever, while in Korea its young shoots are consumed as a vegetable known as “Samnamul” (Lee et al., 2005; Park et al., 2011). Previous phytochemical investigations have identified monoterpenoids, flavonoids such as quercetin and kaempferol, and cyanogenic glycosides from this species. Although antioxidant and cytotoxic activities of *A. dioicus* have been reported, the Vietnamese population of this plant has not been comprehensively studied with respect to its phytochemical profile or its potential hypoglycemic activity.

2. Materials and methods

2.1. Plant Material and Identification

Aerial parts (stems, branches, and leaves) of *A. dioicus* were collected from Quan Lan Island and Van Don District, Quang Ninh Province, Vietnam. The selection of an insular population is noteworthy, as environmental stressors such as salinity and coastal winds may induce the biosynthesis of unique secondary metabolites. Plant materials were air-dried at 40 °C and authenticated by taxonomists at the Institute of Ecology and Biological Resources.



Figure 1. *Aruncus dioicus* collected from Quan Lan Island, Quang Ninh Province, Vietnam.

(A) Natural habitat and whole plant morphology;

(B) Stem and node structure;

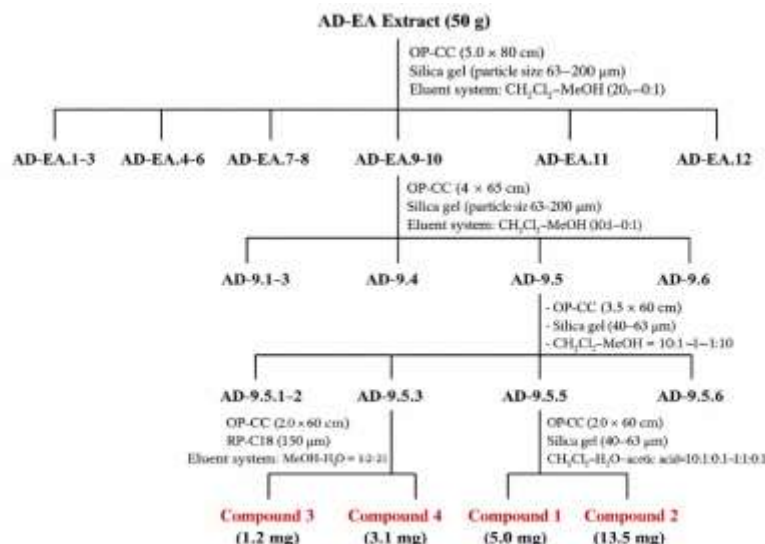
(C) Flowering aerial parts;

(D) Leaves and inflorescences.

2.2. Extraction and Fractionation Protocol

A stepwise extraction method was employed to separate constituents based on polarity.

- Total Extraction:** 2.5 kg of dried powder was extracted with Methanol (MeOH) using ultrasonication at 40°C. Ultrasonication facilitates cell wall disruption via cavitation, enhancing extraction efficiency compared to maceration. This yielded the total methanolic extract (AD-Me, 198.5 g).
- Liquid-Liquid Partitioning:** The AD-Me residue was suspended in water and partitioned sequentially with solvents of increasing polarity:
 - n-Hexane:** Removes lipophilic compounds (fats, waxes, chlorophyll). Yield: AD-Hx (36.7 g).
 - Ethyl Acetate (EtOAc):** Targets medium-polarity compounds such as polyphenols and flavonoids. Yield: AD-EA (52.5 g).
 - Water Residue:** Contains highly polar glycosides and sugars. Yield: AD-H₂O (61.9 g).



Scheme 1. Chromatographic separation and isolation of compounds 1–4 from the AD-EA extract.

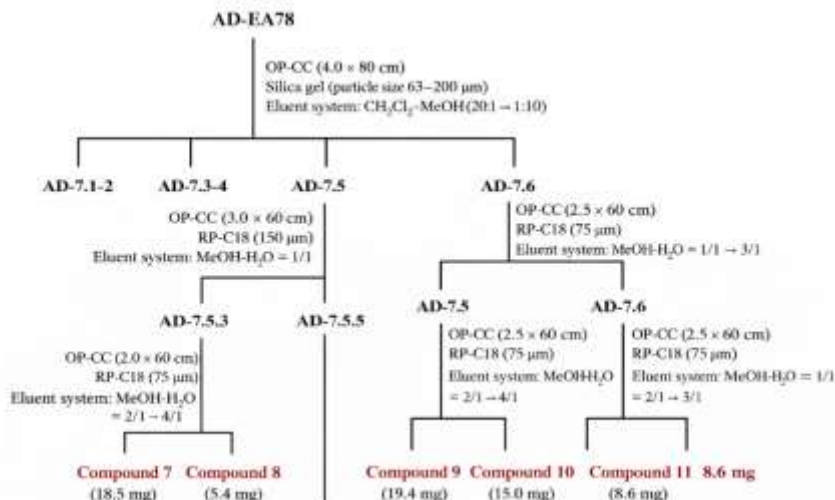
Observation: The high yield of the Ethyl Acetate fraction suggests a significant concentration of polyphenolic compounds, making it the primary focus for isolation.

2.3. Isolation and Purification

The AD-EA fraction (50 g) underwent rigorous separation using Column Chromatography (CC):

- Normal Phase (Silica gel):** Separates compounds based on adsorption/polarity using CH₂Cl₂/MeOH gradients.
- Reversed Phase (RP-18):** Used for finer purification of polar compounds using MeOH/H₂O gradients.

Isolation schemes (Schemes 1 and 2) describe a process of repeated chromatography and Thin Layer Chromatography (TLC) monitoring to obtain 11 pure isolates.



Scheme 2. Chromatographic fractionation and isolation of compounds 6–11 from the EtOAc (AD-EA) subfraction of *Aruncus dioicus*.

2.4. Structural Elucidation

Structures were determined using:

- **Nuclear Magnetic Resonance (¹H-NMR, ¹³C-NMR):** To resolve hydrogen and carbon environments.
- **Literature Comparison:** Spectral data were matched against published values to confirm identity.

2.5. Biological Assays

- **PTP1B Inhibition:** Spectrophotometric assay using *p*-Nitrophenyl Phosphate (*p*-NPP) as a substrate. Ursolic acid served as the positive control.
- **α-Glucosidase Inhibition:** Assay using mammalian enzyme (rat intestine) or yeast enzyme with *p*-nitrophenyl- α-D-glucopyranoside substrate. Acarbose served as the positive control.
- **Data Analysis:** IC₅₀ values were calculated using regression analysis (TableCurve software).

3. Results

3.1. Chemical Characterization Results

Eleven compounds were isolated from the Ethyl Acetate fraction, categorized into Phenylpropanoid glycosides, Phenolic acids, Nucleosides, and Esters.

Table 1. List and scientific names of compounds isolated from *Aruncus dioicus*

No.	Compound code	Scientific name of compound
1	Compound 1	1- <i>O</i> -(4-coumaroyl)-β-D-glucopyranoside
2	Compound 2	1- <i>O</i> -caffeoyl-β-D-glucopyranoside
3	Compound 3	<i>p</i> -Coumaric acid
4	Compound 4	Cinnamic acid
5	Compound 5	Uridine
6	Compound 6	Adenosine
7	Compound 7	Ethylparaben
8	Compound 8	L-(–)-Phenyllactic acid
9	Compound 9	2,4-Dihydroxycinnamic acid
10	Compound 10	Caffeic acid
11	Compound 11	Methyl caffeate

3.2. Pharmacological Results and Discussion

3.2.1. α -Glucosidase Inhibition: Superior Efficacy

Based on the substrate cleavage reaction of *p*-nitrophenyl- α -D-glucopyranoside by the action of the enzyme α -glucosidase, thereby releasing the yellow product *p*-nitrophenol. The enzyme α -glucosidase was obtained from the small intestine of mice, and acarbose (Sigma-Aldrich) was used as the positive control. *p*-Nitrophenyl- α -D-glucopyranoside \rightarrow α -D-glucose + *p*-nitrophenol (yellow).

The amount of *p*-nitrophenol produced 30 minutes after the reaction is reflected by the absorbance of the reaction mixture at a wavelength of 410 nm, representing the activity of the enzyme α -glucosidase.

The method for testing the inhibitory activity of the enzyme α -glucosidase was performed on a 96-well plate (200 μ L/well). Specifically, the sample was diluted with sterile distilled water or 100% DMSO solvent to target concentrations of 1, 4, 16, 64, 256, and 1024 μ g/mL. The positive control used in the experiment was acarbose, while the negative control contained reaction buffer instead of the test sample.

The test sample was incubated at 37 °C. After 30 minutes, the reaction was stopped by adding 100 μ L of Na₂CO₃. The absorbance of the reaction was measured using a Tecan Genios instrument at a wavelength of 410 nm (A).

Table 2. Inhibitory effects of extracts from *Aruncus dioicus* on α -glucosidase activity

No.	Sample name	Inhibitory concentration (IC ₅₀ , μ g/mL ^a)	Type of inhibition
1	Crude extract (AD-Me)	187.6 \pm 3.4	Not determined
2	<i>n</i> -Hexane extract (AD-Hx)	239.3 \pm 2.4	Not determined
3	EtOAc extract (AD-EA)	198.5 \pm 3.7	Not determined
4	Aqueous extract (AD-H ₂ O)	> 250	Not determined
5	Acarbose ^b	154.5 \pm 1.8	Mixed-competitive

Notes:

^a IC₅₀ values represent the concentration required to inhibit 50% of enzyme activity, expressed in μ g/mL.

^b Positive control used in the assay.

The inhibitory capacity of the test sample on alpha-glucosidase enzyme is determined as follows:

$$\text{Inhibition (\%)} = \frac{A_{\text{negative control}} - A_{\text{sample}}}{A_{\text{negative control}}} \times 100$$

Where: IC₅₀ (half maximal inhibitory concentration - calculated using the Table curve software) is the concentration of the test substance that inhibits 50% of the activity of the α -glucosidase enzyme.

Similarly, in this biological activity evaluation experiment, the compound Acarbose was used as a positive control. This is a compound that inhibits the α -glucosidase enzyme and has been used as a positive control in many previous studies. Test samples are considered active when they have the ability to inhibit at concentrations <100 μ M. From there, the IC₅₀ value of the active compounds is calculated using regression analysis. Compounds with IC₅₀ values less than 10 μ M are considered to have strong activity, while those with IC₅₀ values between 10 and 20 μ M are considered to have potential activity. Compounds with IC₅₀ values between 20 and 50 μ M are considered to have moderate activity, while those with IC₅₀ -100 μ M are considered to have weak activity. All other compounds with IC₅₀ values greater than 100 μ M are considered to have no activity.

Table 2 shows the inhibition results of the total extract and fractionated extract samples as shown by their IC₅₀ values in μ g/mL. Of these, the total extract (AD-Me) had the strongest inhibitory value, IC₅₀ = 187.6 \pm 3.4 μ g/mL, followed by the EtOAc extract (AD-EA) with an IC₅₀ value of 198.5 \pm 3.7 μ g/mL. The positive control, Acarbose, had an inhibitory activity value of IC₅₀ = 154.5 \pm 1.8 μ g/mL. The remaining two extract fractions, AD-Hx and AD-H₂O, were considered to have weak inhibitory activity with calculated IC₅₀ values of 239.3 \pm 2.4 and > 250 μ g/mL, respectively.

For the isolated compound samples tested for inhibitory activity against the α -Glucosidase enzyme strain. Table 3 summarizes the results of evaluating this effect.

Table 3. Results of inhibitory activity against the α -Glucosidase enzyme of the compound samples (I-11) isolated from *A. Dioicus*

No.	Compound name	Inhibitory activity (IC ₅₀ , μ M ^a)
1	Compound 1 (1- <i>O</i> -(4-coumaroyl)- β -D-glucopyranoside)	> 250
2	Compound 2	> 250

	(1- <i>O</i> -caffeoyl- β -D-glucopyranoside)	
3	Compound 3 (coumaric acid)	29.62 \pm 0.96
4	Compound 4 (cinnamic acid)	28.58 \pm 0.01
5	Compound 5 (uridine)	133.07 \pm 0.96
6	Compound 6 (adenosine)	183.13 \pm 1.22
7	Compound 7 (ethylparaben)	23.88 \pm 0.47
8	Compound 8 (L-(-)-phenyllactic acid)	147.23 \pm 1.03
9	Compound 9 (2,4-dihydroxycinnamic acid)	45.50 \pm 0.50
10	Compound 10 (caffeic acid)	–
11	Compound 11 (methyl caffeate)	–

Of the 11 tested compounds, five showed inhibitory activity against the α -glucosidase enzyme, namely compounds 3-4, 7-9. Among these, compounds 3 (coumaric acid), 4 (cinnamic acid), 7 (ethylparaben), and 9 (2,4-Dihydroxycinnamic acid) exhibited the strongest inhibitory effects, with IC_{50} values ranging from 23.88 to 45.50 μ M. These values indicate that the activity of these compounds is 4-5 times stronger than that of acarbose – the positive control used in this experiment. Compounds 5 (uridine) and 8 (L-(-)-Phenyllactic acid) were considered to have strong inhibitory activity with IC_{50} values of 133.07 and 147.23 μ M, respectively, equivalent to and slightly higher than acarbose – the positive control – which had an IC_{50} inhibitory value of 154.5 \pm 1.8 μ M. Compounds 1 (1-*O*-(4-coumaroyl)- β -D-glucopyranoside) and 2 (1-*O*-caffeoyl- β -D-glucopyranoside) showed weak inhibitory activity or no inhibitory effect, as evidenced by their IC_{50} inhibitory values $>$ 250 μ M.

The remaining compounds 10 (caffeic acid) and 11 (methyl caffeate) were not evaluated for activity in this test.

3.2.2. PTP1B Inhibition: Identification of Potent Inhibitors

The inhibitory effect on PTP1B enzyme activity was evaluated by the percentage of inhibition at different appropriate concentrations and is listed in Table 4.

The experiments were conducted in triplicate. The mean and mean errors of the results were calculated based on these experimental results using Excel software.

Test samples showed activity when they were able to inhibit at concentrations below 200 μ g/mL. From this, the IC_{50} values of the active test samples were calculated using regression analysis. Test samples with IC_{50} values less than 100 μ g/mL were considered to have strong inhibitory activity with high biological potential, while test samples with values $200 > IC_{50} > 100$ μ g/mL were considered to have moderately strong inhibitory activity.

Test samples with IC_{50} values $>$ 200 μ g/mL were evaluated as having weak activity or were considered ineffective.

In this method, ursolic acid (UA) was used as a positive control. Ursolic acid is a naturally occurring triterpene found in many plant species, notably in the medicinal herbs such as *Morinda officinalis*, *Morinda citrifolia* (*Morinda* spp.), *Orthosiphon stamineus* (cat's whiskers), and *Diospyros kaki* (persimmon), among others.

In this experiment, UA showed high inhibitory activity of the enzyme PTP1B with an IC_{50} value of 3.5 \pm 0.2 μ M

Table 4. Inhibitory activity of extracts from *Aruncus dioicus* against PTP1B

No.	Sample name	Inhibitory concentration (IC_{50} , μ g/mL) ^a	Inhibition type
1	Crude extract (AD-Me)	157.8 \pm 1.4	Not determined
2	<i>n</i> -Hexane extract (AD-Hx)	196.3 \pm 1.7	Not determined
3	Ethyl acetate extract (AD-EA)	133.2 \pm 0.9	Not determined
4	Aqueous extract (AD-W)	$>$ 200	Not determined
5	Ursolic acid ^b	3.5 \pm 0.2	Mixed-competitive

Note:

a) 50 percent inhibitory concentration values in $\mu\text{g/mL}$;

b) Positive control used in the experiment.

All tested extracts showed inhibitory activity against this enzyme strain. Table 4 summarizes the results of evaluating the inhibitory activity of the total MeOH extract from the medicinal plant on the PTP1B enzyme. The total extract showed inhibitory activity with an IC_{50} value of $157.8 \pm 1.4 \mu\text{g/mL}$, and the extracts separated from the total extract fraction, including the n-Hexane extract (AD-Hx), the EtOAc extract (AD-EA), and the water fraction (AD-W), showed inhibitory activity with IC_{50} values of 196.3 ± 1.7 , 133.2 ± 0.9 , and $> 200 \mu\text{g/mL}$, respectively. This demonstrates that the EtOAc (AD-EA) extract inhibited the PTP1B enzyme activity better than the other extracts from the studied goat's beard material.

For the tested pure compounds, Table 5 summarizes the results of evaluating the PTP1B enzyme inhibitory activity of the isolated compounds.

Table 5. PTP1B inhibitory activity of compounds isolated from *Aruncus dioicus*

No.	Compound	Concentration (μM)	Inhibition (%)		Mean \pm SD	IC_{50} (μM)
			Rep. 1	Rep. 2		
1	Compound 1	200	67.52	66.70	67.11 ± 0.43	128.89 ± 0.14
		100	43.01	42.64	42.84 ± 0.19	
		50	17.10	18.01	17.55 ± 0.47	
2	Compound 2	200	72.10	71.05	71.57 ± 0.54	116.66 ± 0.21
		100	45.65	44.77	45.21 ± 0.42	
		50	18.12	20.11	19.13 ± 0.91	
3	Compound 3	10	96.26	98.35	97.30 ± 1.01	0.25 ± 0.19
		1.0	79.87	84.74	82.31 ± 2.11	
		0.1	44.82	45.32	45.07 ± 0.24	
4	Compound 4	100	97.67	97.86	97.76 ± 0.01	1.16 ± 0.10
		10	80.14	83.87	82.00 ± 1.81	
		1	49.43	48.36	48.89 ± 0.54	
5	Compound 5	100	76.84	77.55	77.18 ± 0.32	34.26 ± 0.31
		20	44.18	43.76	43.97 ± 0.26	
		4	17.25	19.34	18.29 ± 1.01	
6	Compound 6	100	87.34	88.36	87.85 ± 0.51	12.25 ± 0.69
		20	64.14	62.29	63.21 ± 0.91	
		4	34.95	33.80	34.37 ± 0.52	
7	Compound 7	100	65.46	65.55	65.51 ± 0.04	47.94 ± 0.01
		20	41.70	41.67	41.68 ± 0.02	
		4	11.75	13.29	12.51 ± 0.71	
8	Compound 8	200	75.88	72.10	73.99 ± 1.89	123.09 ± 0.62
		100	42.39	42.91	42.65 ± 0.25	
		50	18.80	21.10	19.95 ± 1.15	
9	Compound 9	200	70.68	71.12	70.90 ± 0.23	115.80 ± 0.82
		100	46.13	43.50	44.81 ± 1.31	
		50	14.78	15.48	15.13 ± 0.31	
10	Compound 10	100	87.57	85.55	86.55 ± 1.10	11.08 ± 0.92
		20	61.56	63.78	62.67 ± 1.15	
		4	40.83	39.48	40.16 ± 0.63	
11	Compound 11	100	91.24	95.20	93.21 ± 1.97	7.40 ± 0.99
		20	76.64	77.16	76.90 ± 0.25	
		4	42.77	37.70	40.24 ± 2.51	

Of the 11 compounds, 7 showed high inhibitory activity, namely compounds 3-7, 10-11. Notably, compounds 3 and 4 exhibited the highest inhibitory effects, with IC_{50} values of 0.25 and 1.16 μM , respectively. Compound 3, at a concentration of only 10 μM , achieved an inhibition rate of 97.30% for the PTP1B enzyme. Compounds 5, 6, 10, and 11 showed strong inhibitory effects with IC_{50} values ranging from 7.40 to 34.26 μM . Compounds 1, 2, 8, and 9 showed moderate inhibitory activity, with IC_{50} values greater than 100 μM .

4. Discussion

4.1. High Potency of Simple Phenolics

The most significant finding is the strong inhibitory activity of *p*-coumaric acid against PTP1B. With an IC_{50} value of 0.25 μ M, this compound is much more potent than the triterpenoid reference compound ursolic acid ($IC_{50} = 3.5 \mu$ M), which is commonly reported as an effective natural PTP1B inhibitor. Similar micromolar PTP1B inhibition by phenolic acids has been reported in previous studies, although submicromolar activity is less common (Goldstein, 2001; Liu et al., 2022).

This finding implies that the small and planar molecular structure of *p*-coumaric acid contributes towards easier access towards the catalytic site of PTP1B. Its small molecular weight means that the compound would fit into the enzyme pocket and interact with the key catalytic residue, Cys215, which is important for the catalytic activity of the enzyme (Sun et al., 2016).

4.2. Structure-Activity Relationship (SAR):

The 4-OH effect: A comparison of *p*-coumaric acid (0.25 μ M) to cinnamic acid (1.16 μ M) demonstrates that the hydroxyl group on position 4 (para) is critical for the PTP1B inhibition. The 4-OH group has a larger correlating effect on the inhibition of PTP1B. This has also documented for other phenylpropanoid compounds, which demonstrates the effect of para-hydroxyl substitution on PTP1B inhibition (Kim et al., 2006)

Detrimental 3-OH: A reduction of inhibitory activity occurs with the presence of the additional hydroxyl group at the meta (3) position, as in caffeic acid ($IC_{50} = 11.08 \mu$ M).

This indicates that the 3-OH group may obstruct the enzyme pocket binding of the compound. Other phenolic compounds have shown a similar reduction in activity due to over-hydroxylation (Hanhineva et al., 2010).

- **Position 2,4 Substitution:** 2,4 Dihydroxycinnamic acid has shown weak activity against PTP1B ($IC_{50} > 100 \mu$ M). This case reveals that substitution at the ortho (2) position is not ideal for significant inhibitory activity. The 2-OH group may induce steric hindrance or a negative interaction that obstructs binding to the active site of the enzyme.
- **Glycosylation:** The phenylpropanoid glycoside (Compounds 1 and 2) were inactive ($IC_{50} > 100 \mu$ M). This indicates that a glucose moiety is too large and occludes the enzyme catalytic site. Previous studies reported that glycosylation reduces PTP1B inhibitory activity due to the increased size and polarity of the molecule (Zhang & Zhang, 2007).

5. Recommendations and Conclusions

5.1. Recommendations

- **In Vivo Validation:** Given the superior in vitro potency, validation in diabetic animal models (e.g., db/db mice or STZ-induced rats) is essential to evaluate bioavailability and the resultant systemic glucose-lowering effects.
- **Molecular Docking:** Virtual screening will enable the constructive analysis of the the binding processes of Coumaric acid with PTP1B and Ethylparaben with α -glucosidase thus explaining the molecular basis for the strength of their interaction.
- **Product Development:** The high availability of *A. dioicus* in Quang Ninh indicates that the ethyl acetate fraction can also be used for developing standardized herbal supplements aimed at metabolic syndrome.

5.2. Conclusions

This is the first comprehensive study for both its phytochemical and biological aspects of *Aruncus dioicus* from Vietnam with emphasis on the possible antidiabetic effect.

- **Phytochemistry:** The major phenolic acids and phenylpropanoid constituents were found in the ethyl acetate fraction from which eleven compounds were isolated.
- **Pharmacology:** A number of isolated compounds were found to have good in vitro potency against the relevant glucose metabolic enzymes. Among these, *p*-coumaric acid ($IC_{50} = 0.25 \mu$ M) and cinnamic acid ($IC_{50} = 1.16 \mu$ M) were shown to be strong PTP1B inhibitors and ethylparaben, cinnamic acid and *p*-coumaric acid were less active than the reference inhibitors but with respect to α -glucosidase they were strongly active.
- **Dual Inhibitory Potential:** *A. dioicus* extracts may exhibit in vitro dual inhibitory potential, relevant to the management of insulin resistance and postprandial hyperglycemia, as evidenced by the identification of cinnamic acid and *p*-coumaric acid as dual inhibitors of PTP1B and α -glucosidase.

References

1. American Diabetes Association. (2026). *Diagnosis and classification of diabetes: Standards of care in diabetes—2026*. Diabetes Care, 49(Suppl. 1), S27–S49. <https://doi.org/10.2337/dc26-S002>
2. Chen, F., Zhang, X., Wang, J., Wang, F., & Mao, J. (2024). *p*-Coumaric acid: Advances in pharmacological research based on oxidative stress. *Current Topics in Medicinal Chemistry*, 24(5), 416–436. <https://doi.org/10.2174/0115680266276823231230183519>
3. Eldeen, I. M. S., Elgorashi, E. E., & Van Staden, J. (2010). In vitro antidiabetic effects of phenolic compounds from medicinal plants. *Journal of Ethnopharmacology*, 131(3), 521–527. <https://doi.org/10.1016/j.jep.2010.07.043>
4. Goldstein, B. J. (2001). Protein-tyrosine phosphatase 1B (PTP1B) as a therapeutic target for type 2 diabetes and obesity. *Current Drug Targets*, 2(4), 325–335. <https://doi.org/10.2174/1389450013348517>
5. Hanhineva, K., Törrönen, R., Bondia-Pons, I., Pekkinen, J., Kolehmainen, M., Mykkänen, H., & Poutanen, K. (2010). Impact of dietary polyphenols on carbohydrate metabolism. *International Journal of Molecular Sciences*, 11(4), 1365–1402. <https://doi.org/10.3390/ijms11041365>
6. Kashtoh, H., & Baek, K.-H. (2022). Recent updates on phytoconstituent alpha-glucosidase inhibitors: An approach towards the treatment of type two diabetes. *Plants*, 11(20), 2722. <https://doi.org/10.3390/plants11202722>
7. Kim, J. H., Kim, Y. S., Lee, J. Y., & Kang, S. S. (2006). Inhibition of protein tyrosine phosphatase 1B by phenolic compounds isolated from natural sources. *Bioorganic & Medicinal Chemistry Letters*, 16(7), 1934–1937. <https://doi.org/10.1016/j.bmcl.2006.01.021>
8. Lebovitz, H. E. (1997). Alpha-glucosidase inhibitors as agents in the treatment of diabetes. *Diabetes Reviews*, 5, 132–145.
9. Li, Y., Ding, Y., Min, L., & Li, J. (2014). Cinnamic acid derivatives as potential antidiabetic agents: Design, synthesis, and biological evaluation. *European Journal of Medicinal Chemistry*, 76, 306–315. <https://doi.org/10.1016/j.ejmech.2014.02.034>
10. Liu, Y., Zhang, X., Ding, Y., Wang, S., & Li, Z. (2022). Protein tyrosine phosphatase 1B inhibitors from natural products: Recent advances and structure–activity relationships. *Biomedicine & Pharmacotherapy*, 149, 112872. <https://doi.org/10.1016/j.biopha.2022.112872>
11. Rath, S., Dash, R., Mishra, S. K., & Sahoo, C. R. (2022). Natural polyphenols as protein tyrosine phosphatase 1B inhibitors: Insights into structure–activity relationships. *Molecules*, 27(7), 2212. <https://doi.org/10.3390/molecules27072212>
12. Sun, H., Tonks, N. K., & Barford, D. (2016). Protein tyrosine phosphatase 1B: Structure, function, and therapeutic potential. *Trends in Biochemical Sciences*, 41(7), 552–566. <https://doi.org/10.1016/j.tibs.2016.04.002>
13. Tundis, R., Loizzo, M. R., & Menichini, F. (2010). Natural products as alpha-glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: An update. *Mini-Reviews in Medicinal Chemistry*, 10(4), 315–331. <https://doi.org/10.2174/138955710791331007>
14. Zabolotny, J. M., Kim, Y.-B., Welsh, L. A., Kershaw, E. E., Neel, B. G., & Kahn, B. B. (2002). Protein-tyrosine phosphatase 1B regulates leptin signal transduction in vivo. *Developmental Cell*, 2(4), 489–495. [https://doi.org/10.1016/S1534-5807\(02\)00148-X](https://doi.org/10.1016/S1534-5807(02)00148-X)
15. Zhang, Z.-Y., & Zhang, S. (2007). Protein tyrosine phosphatase 1B as a drug target: Recent developments in PTP1B inhibitor discovery. *Drug Discovery Today*, 12(9–10), 373–381. <https://doi.org/10.1016/j.drudis.2007.03.011>