THESIS SUMMARY

Full Name of the Ph.D. Candidate: **Pham Thi Lan**

Thesis Title: **The Study of the Anti-Diabetic Effects of *Mimosa Pudica* L. Leaves in Experimental Models**

Major: **Pharmacology – Clinical Pharmacy** Code: **9720205**

Full Name of Supervisor:

Supervisor 1: **Assoc. Prof. Dr. Bui Thanh Tung**

Supervisor 2: **Assoc. Prof. Dr. Pham Thi Nguyet Hang**

Training Institution: **National Institute of Medicine Materials**

Summary of Thesis Content:

1. Objective

- Evaluate the hypoglycemic effect and various effects related to diabetes of *Mimosa Pudica* L. leaves extract in experimental models.
- Evaluate of the anti-diabetic mechanisms of the extract and two compounds extracted from *Mimosa Pudica* L. leaves through in vitro and in silico studies.

2. Methods

The thesis employed a combination of in vivo, in vitro, and in silico research methods, which are widely recognized and advanced methodologies globally and highly reliable methodologies.

2.1. Oral Glucose Tolerance Test (OGTT) Method

– Evaluate the blood glucose-lowering effects of the total extract and fractions of *Mimosa pudica* leaves using the Oral Glucose Tolerance Test (OGTT) method in normal mice.

– Evaluate the the blood glucose-lowering effects of the total ethanol extract and the n-hexane, ethyl acetate (EtOAc), and butanol (BuOH) fractions of *Mimosa pudica* at a dose of 100 mg/kg b.w. Subsequently, the most effective fraction will be subjected to a repeat OGTT experiment at doses of 50 mg/kg and 100 mg/kg.

2.2. Method for Evaluating the Effects of the Most Effective Fraction in a Type 2 Diabetes Mellitus (T2DM) Mouse Model Induced by a High-Fat Diet and Streptozotocin (STZ):

– Evaluating the blood glucose-lowering effects and improvement in renal function of the ethyl acetate fraction of *Mimosa pudica* leafves extract in a T2DM mouse model induced by a high-fat diet and streptozotocin. Evaluating parameters including blood glucose levels; determining concentrations of triglycerides, total cholesterol, LDL, HDL in the blood, and serum creatinine.

– Evaluating the morphological structure of renal histopathology then to assess the improvement in kidney damage in mice induced with T2DM by STZ.

2.3. Method for Evaluating the Inhibitory Effects on α-Glucosidase and PTP-1B Enzymes of Isolated Compounds from *Mimosa pudica* L. through *In Silico* Modeling:

- Evaluating the inhibitory effects on α-glucosidase and PTP-1B enzymes of the main compounds isolated from *Mimosa pudica*, including Protocatechuic Acid and Syringic Acid, using *in silico* methods to predict the drug-likeness of these compounds.
- These two compounds were extracted from the EtOAc fraction, which has demonstrated the most effective blood glucose-lowering effects fractions. This *in silico* approach aids in predicting the mechanism of action of this fraction in the treatment of type 2 diabetes.
- The method also assists in predicting the absorption, distribution, metabolism, excretion, hepatotoxicity, and dermal toxicity of the two compounds, providing insights into their overall toxicological profiles.

2.4. Evaluation of Inhibitory Effects on α-Glucosidase and PTP-1B Enzymes by Compounds Isolated from *Mimosa pudica* L. *in vitro*

– This method allows for the assessment of the inhibitory effects of compounds isolated from *Mimosa pudica* L. on α-glucosidase and PTP-1B enzymes in vitro, expressed as IC_{50} values, and utilizes positive controls for comparison and clarification.

2.5. Evaluate the inhibitory effects of the EtOAc fraction and two compounds on glucose toxicity on HUVECs; inhibition of AGEs formation caused by MGO; effects of the EtOAc fraction and two compounds on the MGO-AGEs breaker assay (MGO-AGEs breakdown) *in vitro*.

- The protective effects against MGO-induced damage under high glucose conditions by the EtOAc fraction and two compounds were elucidated through *in vitro* experiments on HUVECs cells.

3. Results

3.1. The the hypoglycemic effect and various effects related to diabetes of *Mimosa pudica* L. leaves extract in experimental models.

– The EtOAc fraction of the *Mimosa pudica* L. leaves extract (MP-E, at doses of 50 and 100 mg/kg) demonstrated a blood glucose-lowering effect in the OGTT test.

– The effects of EtOAc fraction on mice induced with type 2 diabetes by a high-fat diet and STZ, after 60 days of treatment, doses of 50 mg/kg/day and 100 mg/kg/day of the EtOAc fraction exhibited significant effects. These effects included a notable reduction in blood glucose levels, improvement in blood lipid profiles, enhancement of kidney function-related indices, reduction in inflammation, attenuation of oxidative stress, and significant

improvement in the histopathological structure of the kidney in the type 2 diabetes-induced mouse model by a high-fat diet and STZ.

3.2. The anti-diabetic mechanisms of the extract and two compounds extracted from *Mimosa pudica* L. leaves

- In this study, we evaluated the inhibitory effects of compounds protocatechuic acid and syringic acid from the *Mimosa pudica* L. leaves extract on enzymes related to the diabetes mechanism. The research results demonstrated that both compounds exhibited strong inhibitory activity against α-glucosidase and PTP-1B, which are crucial targets in diabetes treatment.
- The protective effects against MGO-induced damage under high blood glucose conditions, inhibition of AGEs formation from MGO, and the MGO-AGEs breakdown (MGO-AGEs breaker) on HUVECs cells by the EtOAc fraction and two compounds were also elucidated through in vitro experiments.
- The proposed mechanisms of the blood glucose-lowering effects of EtOAc fraction of the *Mimosa pudica* L. leaves extract may involve the inhibition of α-glucosidase and PTP-1B enzymes, reduction of oxidative stress (decreased MDA concentration and increased levels of antioxidant markers such as SOD, CAT, GPx in the experimental mice kidney tissue), prevention of diabetic nephropathy complications in experimental type 2 diabetes mice, and improvement in kidney inflammation as evidenced by reduced levels of inflammatory markers TNF-α and IL-1β.

4. Conclusion

4.1. Results of the hypoglycemic effect and various effects related to diabetes of *Mimosa pudica* L. leaves extract in experimental models.

- The EtOAc fraction was identified as having the most significant blood glucose-lowering effect compared to the total extract and other fractions in the OGTT test in normal mice.
- The blood glucose-lowering effect of the EtOAc fraction (at a doses of 50 mg/kg/day and 100 mg/kg/day) was studied in a type 2 diabetes mouse model induced by a high-fat diet and low-dose STZ injection. The reductions in blood glucose were 56.3% and 71.3% at doses of 50 mg/kg/day and 100 mg/kg/day, respectively, compared to the pathological control group with $p < 0.05$.
- Regarding various diabetes-related effects, the thesis also investigated the effects of the EtOAc fraction (at a doses of 50 mg/kg/day and 100 mg/kg/day) on improving blood lipid profiles, kidney function-related indices, oxidative stress markers, antioxidant enzyme, inflammatory, and significantly improving the histopathological structure of the kidney in the type 2 diabetes-induced mouse model by a high-fat diet and low-dose STZ injection. Specifically:
  + **Regarding effects on blood lipid profile:** Reduced TC, TG and LDL-C,

increased HDL-C index, with an increase rate of 10.5% ($p<0.05$) at a dose of 50 mg/kg /day; at a dose of 100 mg/kg/day, it reduced total cholesterol by 6.2%, triglycerides by 9.7% and LDL-C by 35.5% and increased HDL-C by 21.4% when compared to the pathological mouse group. ($p<0.05$).

+ **Regarding the improvement in kidney function-related indices:** EtOAc extract fraction (at a doses of 50 mg/kg/day and 100 mg/kg/day) demonstrated a significant reduction in blood creatinine levels, with decreases of 20.2% and 18.4%, respectively ($p < 0.05$) compared to the pathological control group; reduced microalbuminuria concentration, with reductions of 11.9% and 14.9%, respectively; in addition, the EtOAc extract fraction exhibited the ability to increase urinary creatinine and enhance creatinine clearance coefficient with an increase rate of 10.6% and 23.7%, respectively; 50.6% and 72.1% when compared to the pathological control group ($p<0.05$).
+ **Regarding the anti-inflammatory and antioxidant effects on mouse kidney tissue:** The thesis also assessed the effects of the EtOAc fraction (at a doses of 50 mg/kg/day and 100 mg/kg/day) in improving related indices as follows: It significantly reduced the concentration of TNF-α by 17.7% and 24.1%, and IL-1β by 10.3% and 22.2%, respectively, compared to the pathological control group ($p < 0.05$). The EtOAc fraction also decreased the concentration of the lipid peroxidation marker (MDA) by 15.8% and 26.3%, while increasing the levels of antioxidant substances such as SOD, CAT, and GPx by 61.1% and 100%, 29.4% and 59.8%, and 24.7% and 45.6%, respectively, compared to the pathological control group ($p < 0.05$).
+ **Regarding the effects on histopathological changes in the kidney tissue:** The EtOAc fraction (at a doses of 50 mg/kg/day and 100 mg/kg/day) effectively prevented renal damage and significantly improved the histopathological structure of the kidney in the type 2 diabetes-induced mouse model.

4.2. Results of Anti-Diabetic Mechanisms Effects of the EtOAc Fraction of *Mimosa pudica* L. leaves extract and Two Compounds Extracted EtOAc Fraction in vitro and in silico.

– The EtOAc fraction and two compounds demonstrated the potential to mitigate the toxicity of glucose and metabolic dysfunction caused by MGO, related to AGEs targets on HUVEC cells. The blood glucose-lowering mechanism of the EtOAc fraction on mice induced with type 2 diabetes by a high-fat diet and STZ involves reducing inflammation and enhancing antioxidant capacity to improve diabetic nephropathy complications.

– The two compounds, protocatechuic acid and syringic acid, exhibited inhibitory effects on both PTP-1B and α-glucosidase targets. Specifically, protocatechuic acid and syringic acid showed potent inhibitory activity against PTP-1B with IC_{50} values of 248.83 ± 7.66 µM and 450.31 ± 7.77 µM, respectively. Additionally, protocatechuic acid and syringic acid

demonstrated inhibitory activity against α-glucosidase with IC_{50} values of 416.17 ± 9.41 µM and 490.78 ± 9.28 µM, respectively.

Ha Noi, 15 February 2024

SUPERVISORS **PH.D. CANDIDATE**

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