EVALUATING BIOACTIVITIES OF VIETNAMESE HERBALS FOR ANTIDIABETICS AND ITS LONG-TERM COMPLICATIONS

● HA CAM ANH

ABSTRACT:

In this study, the ethanol extracts of three medicinal plants are tested for α-glucosidase inhibitory activity. The degree of α-glucosidase inhibitory activity is determined by measuring the absorbance spectrophotometrically at 405 nm in order to reduce the formation of para-nitrophenol. Medicinal plants including Artocarpus altilis (Park.) Fosb. (A. *altilis*), *Psidium guajava* L. (P.*guajava*), *Gomphrena celosioides Mart.* (G. *celosioides*) are selected based on traditional medicine. The results show that the P. guajava has a strong ability to inhibit α-glucosidase with an IC_{50} value of up to 1.98 µg/mL, compared to acarbose of 1.57 µg/mL. In addition, P. *guajava* and G. *celosioides* show the best potential for xanthine oxidase inhibitory and antioxidant activity, compared to the others, which promises to be applied in the treatment of gout.

Keywords: diabetes, α-glucosidase, medicinal herbs, anti-inflammatory, antioxidant.

1. Introduction

Diabetes mellitus, or diabetes, is an endocrine disorder disease characterized by a hereditary or acquired deficiency in insulin excretion as well as reduced responsiveness of the organs to the insulin produced [1]. According to data from the International Diabetes Federation, there were around 463 million individuals with diabetes in 2019, with the number expected to rise to 630 million by 2045. [2,3]. Long-term consequences in patients with diabetes mellitus include poor wound healing, retinopathy, atherosclerosis, cataract, neuropathy, nephropathy, and impaired wound healing. [4]. Therein, inflammatory and oxidant is the most common complication with diabetes [5]. Therefore, finding medicine or drug for treating diabetes and its complications is always a trend in the world [1]. Natural substances with anti-diabetic effects drew a lot of interest in these attempts. The fundamental disadvantage of herb-based therapy is that plant bioactivities are dependent on extract conditions, hence practically all bioactivities are only visible under the right extract circumstances. Traditional medicine was used to find a remedy to the problems. For example, in traditional Vietnamese medicine, several human diseases may be treated with a mix of herbs; one plant is responsible for treating the sickness, while the others are responsible for treating the problems. Furthermore, the development of pharmaceutical

preparations has resulted in a decrease in the number of herbs used in human illness medicine, which is less effective than the old method. This approach has the potential to be more useful in the treatment of human diseases, particularly diabetes. Herbal therapies are also safe and effective in the treatment of ailments, and they might be a source for the development of new drugs [6,7]. A number of herbal-derived substances such as flavonoids, phenols, triterpenoids, and alkaloids have demonstrated substantial antidiabetic effects, and there are over 800 plants used to treat diabetes healing. [8,9]. Therefore, this work aimed to identify medical plants with anti-diabetes potential of A. *altilis*, P.*guajava*, and G. *celosioides* by evaluating in vitro α-glucosidase inhibitory activity of them. Besides, the total phenols content, antioxidant, anti-inflammatory, and antimicrobial activities related to diabetes complications were determined.

2. Material and method

2.1. Materials

Artocarpus altilis (Park.) *Fosb.*, *Psidium guajava* L.and *Gomphrena celosioides Mart.* leaves were harvested from Binh Chanh district, Ho Chi Minh City, Vietnam on 12/2021. The identification is made at the Department of Ecology and Evolutionary Biology of the Faculty of Biology and Biotechnology, Ho Chi Minh City University of Science, Vietnam National University. After harvesting, the samples were rinsed with water, dried at room temperature, and then ground and stored in sealed bags for an experiment.

2.2. Preparation of Extracts

With 500mL EtOH and a solid/liquid ratio of 1/10 (g/mL), 50.00g of PA and GS combination powder was extracted in 2 hours at 50°C with a solid/liquid ratio of 1/10 (g/mL). After that, the extracts were filtered under vacuum using filter paper. The herbal residue was reused for another extraction under the same conditions. Two types of extractions were combined and concentrated at 55°C using rotating vacuum evaporation (Buchi R-215 Rotavapor). All of the experiments were carried out three times.

Qualitative phytochemical screening

Phytochemical screening of the extract of medicinal plants was used to determine the presence of bioactive compounds: polyphenols, flavonoids, alkaloids, and tannins [10-12].

2.3. Determined bioactivities method

The investigation of the α-glucosidase enzyme inhibitory activity of the extract was conducted following Liu's method [13]. The oxidant is one of the main complications of diabetes, thus, finding the agent has antioxidant activities and antidiabetics is required. The antioxidant activity of the sample was investigated by DPPH-free radical scavenging assay according to Stagos's method with slight modifications [14]. The *in vitro* anti-inflammatory activity of these extracts was also evaluated via the extract's protective activity against albumin denaturation as described by the previous studies with slight modifications[15].

2.4. Statistical Analysis

All analyses were done at least in triplicate, and these values were then shown as mean values along with their standard derivations (±SD). The data are expressed as mean values ± standard deviation for each measurement.

3. Results and discussion

3.1. Phytochemical studies of three herbals

Polyphenols, flavonoids, alkaloids, tannins, and other natural substances have been demonstrated to have anti-α-glucosidase enzyme activity. To find bioactive chemicals, phytochemical screening of 3 plants was performed, and the results are displayed in Table 1. Flavonoids, polyphenols, and tannins are present in varying amounts in all extracts. The existence of these distinct bioactive chemicals suggested the possibility of a wide range of biological functions. Polyphenols are secondary metabolites generated by higher plants that have anti-diabetes, antioxidant, anti-inflammatory, anti-carcinogenic, and anti-gout properties. Flavonoids reduce the activity of enzymes involved in the generation of free radicals, such as α-glucosidase, peroxidase, and nitric oxide synthase, resulting in less oxidative damage to macromolecules. Tannins, which are water-soluble polyphenols,

Table 1. The phytochemical screening of *A. altilis*, P. *guajava*, and G. *celosioides* extracts

Bioactive compounds	Test	Extracts		
		A. *altilis*	P. *guajava*	G. *celosioides*
Polyphenol	$FeCl_3$	++	++	++
Flavonoid	Mg/HCl	-	+	+
	Chì acetate 10%	++	++	++
Alkaloid	Bouchardat	+	+	++
	Dragendorff	+	+	++
Tannin	$FeCl_3$	++	++	+
Saponin	Liebermann - Burchard	+	+	-
Cardiac Glycoside	Keller - Kiliani	-	-	-
Carotenoid	H_2SO_4	-	-	-
- Not detected; + Slightly positive reaction; and ++ Strong positive reaction				

contain many bioactivities in vitro, the most well-studied of which are antibacterial and antioxidant capabilities. Alkaloids have powerful biological effects on humans, including anti-inflammatory properties, even though inflammation is the most common gout symptom. Preliminary phytochemical analysis indicates that medicinal plants have the potential to cure diabetes.

3.2. The bioactivities of three herbals.

The results of the bioactivities evaluation of three Vietnam herbals were shown in table 2. The extract of P. *guajava* showed strong inhibitory activity against yeast α-glucosidase with IC_{50} of 1.98 µg/mL, compared to IC_{50} of acarbose of 9.32 µg/mL. Therefore, it could be concluded that the P. guajava had potential in the treatment of type II diabetes. The antioxidant ability of the P. guajava extracts is quite strong with IC_{50} of 17.23 µg/mL compared to that of Vitamin C (IC_{50} of 1.23 µg/mL). Inflammation is a complicated process that involves the reaction of bodily tissues to infection, irritation, or other damage. As a result, inflammation is implicated in a variety of illnesses, including diabetes [31]. The anti-inflammatory activity of the G. *celosioides* extracts reaches a low IC_{20} value of 5.13 µg/mL. According to William et al., extracts with inflammatory inhibition over 20% after albumin denaturation can be regarded as an anti-inflammatory drug [17]. Therefore, it is possible to rely on the albumin denaturation above 20% to assess the potential anti-inflammatory activity of the enriched flavonoid extract. Despite

Table 2. The bioactivities of *A. altilis*, P. *guajava*, and G. *celosioides* extracted with Ethanol solvents

Bioactivities	A. *altilis*	P. *guajava*	G. celosioides	Positive control
α-glucosidase inhibitory (µg/mL) *	35.55 ± 0.045	1.98 ± 0.035	31.42 ± 0.23	9.32 ± 0.17 (Acarbose)
Antioxidation (µg/mL) *	49.30 ± 0.033	17.23 ± 0.13	22.98 ± 0.021	1.23 ± 0.016 (Ascorbic acid)
Anti-inflammatory (µg/mL)**	70.38 ± 0.016	38.96 ± 0.024	5.13 ± 0.38	5.63 ± 0.53 (Diclofenac)
*IC_{50} value ** IC_{20} value				

having lower anti-inflammatory activity with IC_{20} value of 38.96 µg/mL than G. *celosioides*, P.*guajava* can still consider an anti-diabetes and its complication agent due to its high anti-α-glucosidase and antioxidation.

4. Conclusion

The present work evaluated and screened medicinal plants for α-glucosidase inhibitory activity. The extract of P. guajava shows strong α-glucosidase inhibitory activity with an IC_{50} value lower than acarbose (9.32 µg/mL). The P. guajava leaf also showed the best antioxidant activity with the value of IC_{50} of 1.23 µg/mL. In summary, P. guajava leaf could be a good candidate for future studies of this plant in the treatment of diabetes and its complications ■

Acknowledgment:

We acknowledge the support of time and facilities from Ho Chi Minh City University of Technology (HCMUT), VNU-HCM for this study.

REFERENCES:

1. Do NHN, Le TM, Nguyen CDP, Ha AC. (2020). Optimization of total flavonoid content of ethanolic extract of Persicaria pulchra (Bl.) Soják for the inhibition of α-glucosidase enzyme. Fine Chemical Technologies, 15, 39-50.

2. Andersson E, Persson S, Hallin N, Ericsson Å, Thielke D, Lindgren P, et al. (2020). Costs of diabetes complications: hospital-based care and absence from work for 392,200 people with type 2 diabetes and matched control participants in Sweden. *Diabetologia,* 63, 2582-94.

3. Shaw JE, Sicree RA, Zimmet PZ. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice,* 87, 4-14.

4. Ahmed N. (2005). Advanced glycation endproducts-role in pathology of diabetic complications. *Diabetes Research and Clinical Practice,* 67, 3-21.

5. Oguntibeju OO. (2019). Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. *International Journal of Physiology, Pathophysiology and Pharmacology,* 11, 45.

6. Edwards S, Da-Costa-Rocha I, Lawrence MJ, Cable C, Heinrich M. (2012). Use and efficacy of herbal medicines: Part 1-Historical and traditional use. *Pharmaceutical Journal,* 289,161-2.

7. Hung H-Y, Qian K, Morris-Natschke SL, Hsu C-S, Lee K-H. (2012). Recent discovery of plant-derived anti-diabetic natural products. *Natural Product Reports,* 29, 580-606.

8. Sharma B, Salunke R, Balomajumder C, Daniel S, Roy P. (2010). Anti-diabetic potential of alkaloid rich fraction from Capparis decidua on diabetic mice. *Journal of Ethnopharmacology,* 127, 457-462.

9. Yousef F, Yousef N, Mansour O, Herbali J. (2017). Metformin: a unique herbal origin medication. *Global Journal of Medical Research,* 17.

10. De Silva GO, Abeysundara AT, Aponso MMW. (2017). Extraction methods, qualitative and quantitative techniques for screening of phytochemicals from plants. *American Journal of Essential Oils and Natural Products,* 5, 29-32.

11. Kerrouri S, Lrhorfi LA, Amal S, Ouafae E, abdellahi Lella O, Bahia B, et al. (2016). Qualitative study of bioactive components of dill (*Anethum graveolens L.*) from Northern Morocco. *European Scientific Journal,* 12.

12. Nagalingam S, Sasikumar CS, Cherian KM. (2012). Extraction and preliminary phytochemical screening of active compounds in Morinda citrifolia fruit. *Asian Journal of Pharmaceutical and Clinical Research,* 5, 179-181.

13. Liu F, Ma H, Wang G, Liu W, Seeram NP, Mu Y, et al. (2018). Phenolics from Eugenia jambolana seeds with advanced glycation endproduct formation and alpha-glucosidase inhibitory activities. *Food & Function Journal,* 9, 4246-54.

14. Stagos D. (2020). Antioxidant activity of polyphenolic plant extracts. *Antioxidants (Basel),* 9(1), 19.

15. Eshwarappa RSB, Ramachandra YL, Subaramaihha SR, Subbaiah SGP, Austin RS, Dhananjaya BL. (2016). Anti-Lipoxygenase activity of leaf gall extracts of Terminalia chebula (Gaertn.) Retz. (Combretaceae). *Pharmacognosy Research,* 8, 78.

16. Pedersen BK. (2017). Anti-inflammatory effects of exercise: role in diabetes and cardiovascular disease. *European Journal of Clinical Investigation,* 47, 600-11.

17. Williams LAD, O'Connar A, Latore L, Dennis O, Ringer S, Whittaker JA, et al. (2008). The in vitro anti-denaturation effects induced by natural products and non-steroidal compounds in heat treated (immunogenic) bovine serum albumin is proposed as a screening assay for the detection of anti-inflammatory compounds, without the use of animals. *West Indian Medical Journal,* 57.

Received date: May 2, 2022
Reviewed date: May 18, 2022
Accepted date: May 29, 2022

Author information:
ANH C. HA[1,2]
[1]Faculty of Chemical engineering, Ho Chi Minh City University of Technology
[2]Vietnam National University Ho Chi Minh City

ĐÁNH GIÁ HOẠT TÍNH SINH HỌC CỦA MỘT SỐ THẢO DƯỢC VIỆT NAM TRONG ĐIỀU TRỊ BỆNH ĐÁI THÁO ĐƯỜNG VÀ CÁC BIẾN CHỨNG CỦA BỆNH

● TS. **HÀ CẨM ANH[1,2]**
[1]Khoa Kỹ thuật Hóa học, Trường Đại học Bách khoa TP. Hồ Chí Minh (HCMUT)
[2]Đại học Quốc gia TP. Hồ Chí Minh (VNU-HCM)

TÓM TẮT:

Trong nghiên cứu này, dịch chiết ethanol của 3 cây thuốc đã được thử nghiệm về hoạt động ức chế enzyme α-glucosidase. Khả năng ức chế α-glucosidase được xác định bằng cách đo quang phổ hấp thụ ở bước sóng 405 nm để giảm sự hình thành para-nitrophenol. Các cây thuốc được chọn bao gồm *Artocarpus altilis* (Park.) *Fosb.* (A. altilis), *Psidium guajava L.* (P.guajava), *Gomphrena celosioides Mart.* (G. celosioides) dựa trên y học dân gian. Kết quả cho thấy P.*guajava* có khả năng ức chế α-glucosidase mạnh với giá trị IC_{50} lên đến 1,98 µg / mL, so với acarbose là 1,57 µg / mL. Bên cạnh đó, P.*guajava* và G. *celosioides* cho thấy tiềm năng tốt trong hoạt tính ức chế xanthine oxidase và chống oxy hóa so với các loại khác, hứa hẹn sẽ được ứng dụng trong điều trị bệnh gút.

Từ khóa: tiểu đường, α-glucosidase, dược liệu, kháng viêm, kháng oxy hóa.