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Medicinal plants with antidiabetic activity used in traditional medicine in Ecuador

BACHELOR’S THESIS

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Declaration

I hereby declare that I have done this thesis entitled Medicinal plants with antidiabetic activity used in traditional medicine in Ecuador independently, all texts in this thesis are original, and all the sources have been quoted and acknowledged by means of complete references and according to Citation rules of the FTA.

In Prague 20. 7. 2023

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Adéla Flekalová

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Abstract

Diabetes mellitus, characterised by insulin deficiency, is one of the concerning health problems worldwide, especially in developing countries. Due to the systemic toxicity and limited effectiveness of existing antidiabetic medications, there is an urgent need to discover new plant-based natural antidiabetic alternatives. Medicinal plants have historically held significance in managing various health problems, and in recent years, there has been a surge in their global popularity due to their natural origin and minimal side effects, appealing to both developing and developed countries. Ecuador has a rich ethnobotanical heritage, with many indigenous medicinal plants exhibiting hypoglycemic or anti-hyperglycemic properties enriched with bioactive compounds. These medicinal plants have been utilised in traditional Ecuadorian medicine for many decades to manage diabetes, owing to their cost-effectiveness, use of traditional knowledge, and minimal toxicity. However, a notable absence of integrated approaches between existing ethnomedicinal practices and pharmacological research persists. Thus, this review aims to explore Ecuador's traditional medicinal plants employed in diabetes management and their bioactive phytochemicals, which are primarily responsible for their antidiabetic properties.

Key words: antidiabetic properties, bioactive compounds, diabetes, Ecuadorian medicinal plants, ethnobotany

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1. Introduction

Diabetes mellitus (DM) represents a significant public health challenge, driven by escalating rates of obesity and characterized by high rates of comorbidity, diminished quality of life, premature mortality, and substantial economic and societal burdens (Chan et al. 2020). Long-term diabetes can lead to various complications, including microvascular issues such as nephropathy, neuropathy, and retinopathy, as well as macrovascular complications like atherosclerosis, heart attacks, and peripheral vascular disease (Ighodaro 2018; Luna et al. 2021). The prevalence of diabetes has surged at the national, regional, and global levels (Cho et al. 2018). Moreover, the International Diabetes Federation (IDF) projects that by 2030, the number of individuals with DM is anticipated to reach 578 million, surging to 629 million by 2045, resulting in a global prevalence of 9.9% (Aschner et al. 2020).

Additionally, the average prevalence of diabetes in South and Central America reached 9.4% in adults, affecting approximately 32 million people. During this period, Ecuador ranked among the top 20 countries with the highest prevalence of DM at 5.5% (IDF 2021). According to the IDF 2021 study, 4.7% of Ecuadorians aged 20-79 had diabetes, and diabetes ranked as the second-largest cause of mortality in Ecuador in 2021, following COVID-19. Expenses related to diabetes per person are estimated at approximately 2,280 USD annually (Sun et al. 2022). Fragmented healthcare systems and high out-of-pocket health costs impose an enormous financial burden on individuals for effective disease management (Lucio et al. 2011).

Furthermore, with the growing prevalence of DM in rural communities worldwide, along with the detrimental effects of synthetic medicine, there is an imperative need for the development of indigenous, inexpensive botanical sources for anti-diabetic crude or purified drugs. Over the last few decades, several medicinal plants such as *Allium sativa* L., *Trigonella Graecum Foenum*, *Silybum marianus*, *Citrullus colocynthis*, *Zingiber officinale*, etc., have been useful in treating diabetes and are used empirically as anti-diabetic and anti-hyperlipidemic remedies (Eidi et al. 2006; Huseini et al. 2009).

Several Ecuadorian ethnic groups heavily rely on medicinal plants to maintain their health (Herrera-Feijoo et al. 2023). The clinical expertise of traditional healer practitioners has been meticulously maintained over thousands of years (Armijos et al. 2022). Therefore, herbal drugs have gained legitimacy over the years due to the evident efficiency and safety of plants (WHO 2007). Consequently, many health care providers are now combining modern and traditional medicines (Armijos et al. 2022).

Several ethnopharmacological research studies have been conducted in Ecuador. Despite being a multicultural country, there are only few ethnopharmacological studies concerning the treatment of diabetes (Tene et al. 2007; Arumugam et al. 2013). In 2018 Ecuador was ranked last in Latin America in terms of scientific production in ethnobiology field and furthermore the number of articles published about medicinal plants in Ecuador is decreasing every year (González-Rivadeneira et al. 2018).

Several ethnopharmacological research studies have been conducted in Ecuador. However, being a multicultural country, there are only few ethnopharmacological studies focusing on the treatment of diabetes (Tene et al. 2007; Arumugam et al. 2013). In 2018, Ecuador ranked last in Latin America in terms of scientific production in the field of ethnobiology, and furthermore, the number of articles published about medicinal plants in Ecuador has been decreasing annually (González-Rivadeneira et al. 2018).

2. Aims of the Thesis

The main goal of this thesis was to describe the current knowledge of antidiabetic medicinal plants traditionally employed in Ecuador. The research aimed to address the following questions:

1) How many species exhibiting potential antidiabetic properties were identified in Ecuador?
2) How many of the examined plants have had their antidiabetic activity scientifically confirmed?
3) Are people from Ecuador using medicinal plants accordingly?

3. Literature Review

3.1. Ecuador

Ecuador, located in the western part of South America and bordered by the Pacific Ocean along the Equator (Fig. 1), is geographically divided into three main regions Coastal Lowlands (La Costa), the Andean Highlands (La Sierra), and the Amazon Rainforest (El Oriente). Additionally, there exists a fourth distinct area, the Galapagos Islands (Archipelago), located about 1000 kilometres offshore in the Pacific Ocean (Bruhns et al. 2011).

In 2022, Ecuador's population exceeded 18 million, encompassing 13 indigenous nationalities, each characterised by unique languages, histories, and cultures (García-Vélez et al. 2022; González-Rivadeneira et al. 2018). The Ecuadorian population is categorised into five main ethnic groups: Afro-Ecuadorian, Indigenous, Blanco, Mestizo, and Montubio. Mestizos, constituting the largest segment at 71.9%, are descendants of both Europeans and Indigenous Americans, primarily inhabiting urban areas and mostly speaking Spanish. Ecuador is a home to fourteen distinct Indigenous groups, representing 7.0% of the total population (Nagar et al. 2021). Each ethnic group maintains a distinct relationship with the environment, reflected in their unique medical practices that rely on specific medicinal species. The indigenous knowledge they possess is crucial in recognizing the therapeutic efficacy of these plants in treating specific diseases. (Bibi et al. 2014; Tene et al. 2007).

Classified as a middle-income country, Ecuador faced a poverty rate of 25% in 2019 (BTI 2022). However, the Covid-19 pandemic led to a drastic increase, reaching 33%. Poverty started to decline in 2021 but it remains a persistent challenge for Ecuador's economy (García-Vélez et al. 2022). Ecuador's GDP per capita is 6,391 US dollars, ranking among the lowest in South America (World Bank 2022). Approximately 22% of the population earns below $1.90 US dollars per day, mostly involving individuals in rural areas. A significant portion, 36%, resides in medically underserved rural areas where only 14% of public health care is concentrated (Brusnahan et al. 2022). Therefore, use of traditional medicine is provoked (Naranjo & Escaleras 1995).

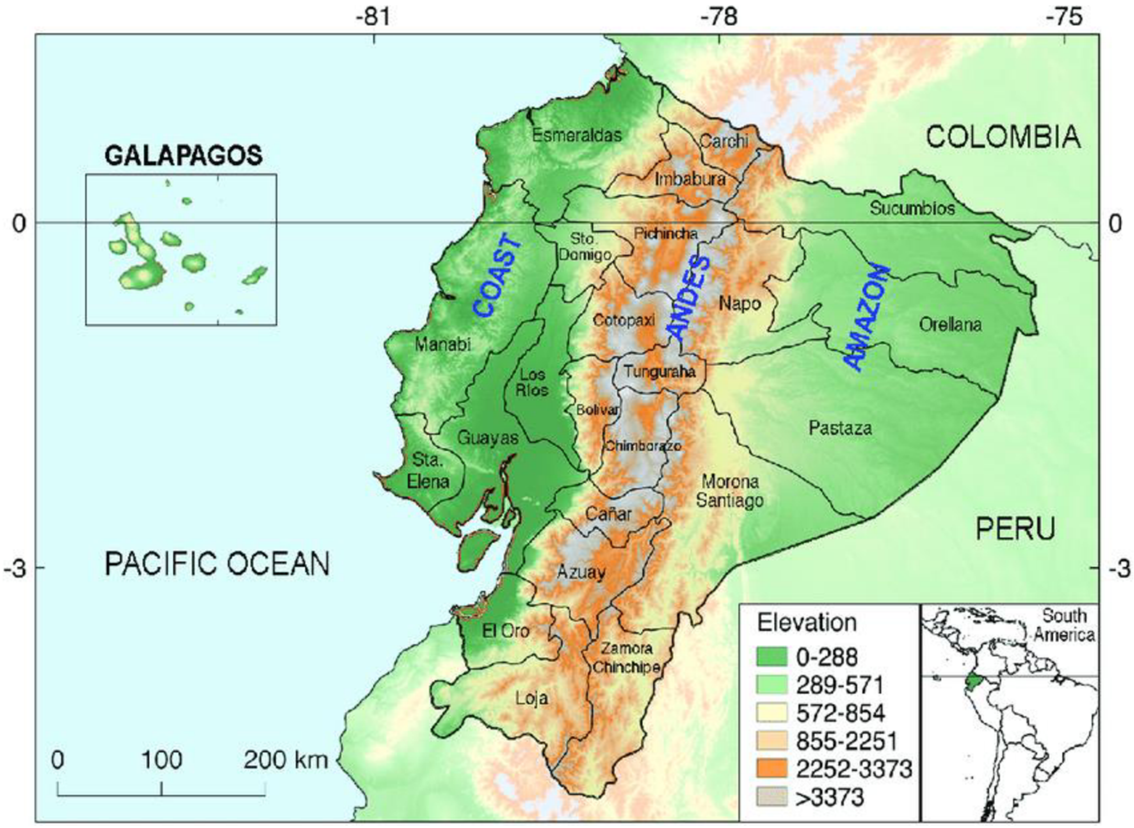

Figure 1. Geographical map of Ecuador

(Source: Calvopiña et al. 2022)

3.2. Traditional medicine

Traditional medicine, particularly herbal remedies, plays a significant role in managing chronic diseases such as diabetes. Globally, nearly 80% of the population relies on plant-based remedies for primary healthcare. Rural communities exhibit essential knowledge regarding plant uses, preferring medicinal plants due to their easy availability and cost-effectiveness compared to expensive pharmaceuticals (Bibi et al. 2014).

Traditional healing practices have been proven beneficial across various countries, regardless of access to conventional allopathic medicine. Within the United States, there's an emerging trend of turning to traditional practices, particularly for conditions resistant to allopathic remedies. An increasing number of individuals is showing interest in the knowledge preserved by traditional healers, as well as in the medicinal plant diversity (Bussmann et al. 2007).

3.3. Diabetes

Diabetes mellitus (DM) is a metabolic disorder characterised by inadequate control of blood glucose levels, affecting approximately 537 million adults globally, with over three-quarters residing in low- and middle-income countries (IDF 2021; Sapra & Bhandari 2023). Various types of diabetes exist, with the most common ones being type 1 and type 2 diabetes, both capable of leading to hyperglycemia, an elevation in blood glucose concentration (Sapra & Bhandari 2023). In type 1 diabetes, insulin production stops, while the more common type 2 diabetes is characterised by insulin resistance, where the insulin produced in the pancreas is inefficiently utilised by the body's tissues. Currently, the most effective approach at managing diabetes involves mitigating postprandial hyperglycemia by inhibiting the activity of carbohydrate hydrolysis enzymes in the digestive system (Abd Elkader et al. 2022).

The use of natural extracts with pharmacological properties has gained significant attention due to their potential therapeutic efficacy in treating various diseases while exhibiting minimal side effects. Elevated blood sugar levels, known as hyperglycemia, contribute to the formation of active free radicals, leading to complications associated with diabetes such as tissue oxidative damage and disorders like nephropathy, neuropathy, retinopathy, and cognitive dysfunction. A key symptom of diabetes is abnormal blood sugar levels, which are caused by the inability of the immune system to produce enough insulin (Abd Elkader et al. 2022). Postprandial hyperglycemia occurs post-meal due to the breakdown of starch by α-amylase and α-glucosidase enzymes, leading to elevated glucose levels. Inhibiting these intestinal enzymes is essential for managing type 2 diabetes. Glucosidase, an essential digestive enzyme, breaks down dietary carbohydrates into simple sugars. Glucosidase inhibitors such as acarbose work by slowing down the digestion of carbohydrates, thereby delaying their absorption from the digestive tract. Therefore, they have the potential to prevent the onset of type 2 diabetes by lowering post-meal glucose levels (Abd Elkader et al. 2022; Liu et al. 2011).

According to the World Health Organization, DM ranks as the fifth leading cause of death for females and seventh for males in Ecuador (Sapra & Bhandari 2023). The International Diabetes Federation reported 526.7 thousand individuals aged 20-79 living with diabetes in Ecuador in 2021. About 63% of the Ecuadorian population is identified as overweight or obese, predominantly represented by women, where obesity rates are three times higher than among men, therefore an increase in the prevalence of type 2 diabetes cases is expected (Puig-García et al. 2023).

In 2015, Latin America and the Caribbean had 41 million adults (20 years and older) with DM. In Ecuador, where there is a 40% poverty rate and fragmented healthcare systems, individuals encounter out-of-pocket health expenses. The estimated diabetes-related costs per person amount to around 2,280 USD per year, imposing a significant financial burden on the population (Puig-García et al. 2023).

3.4. Ethnobotany

Ethnobotany is described as a science combining Anthropology and Botany. Furthermore, it includes phytochemistry, pharmacology, nutrition, and various plant uses within traditional communities. Notably, ethnobotanical studies focus on ecological aspects related to the traditional use of plants, considering their significance to the community's environment or addressing concerns about the irrational use of certain species. This combination of local community wisdom with scientific knowledge in ethnobotany plays a pivotal role in the pursuit of biocultural conservation. Additionally, it contributes to the global transfer of plants from local markets and also to valuing and preserving traditional knowledge (Silveira & Boylan 2023). Furthermore, the study of indigenous medicine helps identify new pharmaceuticals and agrochemicals (Prance 1991). With increasing medicinal plant consumption ethnobotanical studies are currently necessary and important (Tinitana et al. 2016).

According to research made in Loja province in 33 studied markets 160 medicinal species were found. Due to high plant diversity in this area, there are many plants that could potentially contain antidiabetic properties. There were found 57 medicinal plant species sold for treatment of diseases related with digestive, dermatological, and sensorial systems. *Matricaria recutita* and *Gaiadendrum punctatum*, used against digestive and respiratory problems, were found in every market of the area (Tinitana et al. 2016).

3.5. Market of medicinal plants in Ecuador

The economic value of the medicinal plant market was studied in Northern Peru. It revealed that medicinal plants play a crucial role in local economies (Figure 2), generating an estimated annual income of 1.2 million USD. Interestingly, just 10% of all traded species, including seven indigenous and three exotic plants, contribute to over 40% of total sales. Additionally, 31 native species constitute half of all sales, while only 16 introduced plants make up over a quarter of the total material sold. Despite their popularity, none of the exotic species are endangered. However, the increasing demand for these plants may lead to heightened cultivation, which could potentially pose risks to the local flora (Bussmann et al. 2007).

Figure 2. Sale of medicinal plants in Guayaquil, Ecuador

(Source: Barreno 2017)

4. Methodology

The methodology of the bachelor thesis was based on information compiled mainly from available online scientific publications in both English and Spanish in order to obtain the most up-to-date data. The databases like Scopus, ScienceDirect, ResearchGate, SciELO, PubMed and Web of Science were searched using keywords such as traditional medicine of Ecuador, medicinal plants with antidiabetic activity, plants used for treatment of diabetes, ethnobotanical surveys of Ecuador.

Each plant utilised in Ecuador for treating diabetes underwent a selection process, including the collection of data such as family, scientific name, local name (vernacular name), plant part, preparations, habit, origin, and references. Every species' scientific name and family were verified and corrected in accordance with the International Plant Names Index. Habit and origin information were cross-checked and validated using the Plants of the World Online database. Subsequently, all plants were organised alphabetically based on their botanical family and summarised in a final table and accompanying graphs.

5. Medicinal plants with antidiabetic potential used in traditional medicine of Ecuador

Based on the literature reviewed, the study has identified 27 medicinal plants utilised in Ecuadorian traditional medicine for treating Diabetes mellitus, as displayed in Table 1. These plants belong to 23 botanical families, with the most prominent representation coming from families such as Asteraceae, Apiaceae, Costaceae, and Leguminosae, each with two species (7.4% each), followed by 19 families with one species each (Figure 3). Asteraceae, recognized as the most encountered family in ethnobotanical studies globally, exhibits the greatest diversity of species in South America (Bibi et al., 2014; Pekova et al., 2023). Among the identified plants, 15 (56%) are native to Ecuador, while the remaining 12 representatives (44%) were introduced (Figure 4).

Table 1. Medicinal plants with antidiabetic potential used in traditional medicine of Ecuador

Family	Scientific name	Local name (Vernacular name)	Plant part	Preparations	Habit	Origin	References
Acanthaceae	*Justicia colorata* (Nees) Wassh.	Insulina	Leaf, stem	Infusion	Shrub	N	13
Apiaceae	*Foeniculum vulgare* Mill.	Hinojo, *eneldo*	Whole plant	Infusion	Herb	I	2; 4; 12
	Neonelsonia acuminata (Benth.) J.M.Coult. & Rose ex Drude	Zanahoria blanca	Root	Eaten raw	Herb	N	3; 13
Aquifoliaceae	*Ilex guayusa* Loes.	Guayusa	Leaf	Infusion	Tree	N	7; 13
Asteraceae	*Baccharis genistelloides* (Lam.) Pers.	Tres filos	Aerial part	Aqueous infusion	Herb, shrub	N	1; 2; 3; 13; 16
	Matricaria chamomilla L.	Chamomile	Whole plant	Infusion	Herb	I	6; 9
Convolvulaceae	*Ipomoea carnea* Jacq.	Borrachera, matacabra	Aerial part	Infusion	Shrub, tree	N	15
Costaceae	*Costus comosus* Roscoe	Caña	Stem	Decoction	Herb	N	13; 16
	Costus villosissimus Jacq.	Caña agria	Leaf, stem	Infusion	Herb	N	10

Crassulaceae	Bryophyllum gastonis-bonnieri (Raym.-Hamet & H.Perrier) Lauz.-March.	Dulcamara	Leaf	Juice, crushed	Herb	I	11; 17
Euphorbiaceae	*Croton wagneri* Müll.Arg.	Moshquera	Leaf	Aqueous infusion	Shrub	N	16
Fabaceae	Cajanus cajan (L.) Millsp.	Fréjol de palo	Bark	Infusion	Tree	I	15
Geraniaceae	*Pelargonium graveolens* L'Hér.	Esencia de rosa	Flower, leaf, stem	Infusion	Subshrub, shrub	I	4
Juglandaceae	*Juglans neotropica* Diels	Nogal, tocte	Leaf	Infusion	Tree	N	15
Lauraceae	*Persea americana* Mill.	Aguacate	Leaf, fruit, seed	Aqueous infusion, decoction	Tree	I	5; 16
Leguminosae	*Glycyrrhiza glabra* L.	Zaragoza	Leaf, stem	Infusion	Herb, subshrub	I	17
	Myroxylon peruiferum L.f.	Bálsamo, chaquino	Bark	Infusion	Tree	N	15
Mimosaceae	*Pithecellobium excelsum* (Kunth) Mart.	Chaquiro	Bark	Infusion	Tree	N	15
Monimiaceae	*Siparuna eggersii* Hieron.	Monte del oso	Leaf	Crushed, infusion	Shrub, tree	N	13; 16
Moraceae	*Artocarpus altilis* (Parkinson) Fosberg	Fruto del pan	Leaf	Aqueous infusion	Tree	I	13; 16
Piperaceae	*Piper crassinervium* Kunth	Guabiduca	Stem, leaf	Decoction	Shrub, tree	N	13; 16
Proteaceae	*Oreocallis grandiflora* R.Br.	Cucharillo	Leaf, bark, flower	Aqueous infusion	Tree	N	3; 13; 16
Pteridaceae	*Adiantum poiretii* Wikstr.	Culantrillo	Aerial part	Aqueous infusion	Herb	I	3; 13; 16
Rutaceae	*Ruta graveolens* L.	Ruda	Stem, leaf	Infusion	Subshrub	I	6
Solanaceae	Physalis peruviana L.	Uvilla, uchuva, uvilla lanuda	Fruit	Juice	Herb, subshrub	I	4; 8
Urticaceae	*Urtica dioica* L.	Ortiga	Whole plant	Infusion, fresh	Herb	I	6; 14
Verbenaceae	*Verbena litoralis Kunth*	Verbena	Whole plant	Cooked, infusion	Herb	N	2; 13

(N - native, I – introduced)

1 - Aguirre et al. 2014; **2 -** Andrade et al. 2017; **3 -** Armijos et al. 2021; **4 -** Armijos et al. 2022; **5 -** Dabas et al. 2013; **6 -** Dostalíková 2017; **7 -** Dueñas 2016; **8 -** Ezzat et al. 2021; **9 -** Fernandéz et al. 2019; **10 -** Gallegos-Zurita 2016; **11 -** García-Pérez et al. 2020;

12 - Jadid et al. 2023; **13 -** Jaramillo-Fierro et al. 2018; **14 -** Mehri et al. 2011; **15 -** Motto 2005; **16 -** Tene et al. 2007; **17 -** Zambrano-Intriago 2015

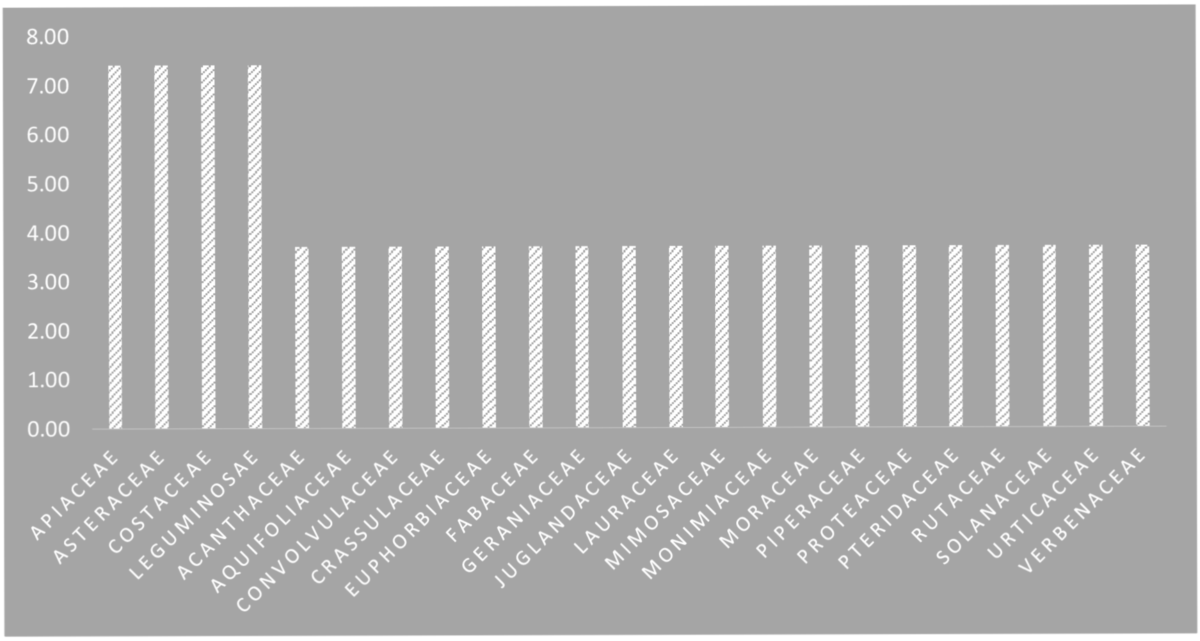

Figure 3. Botanic family representation (%)

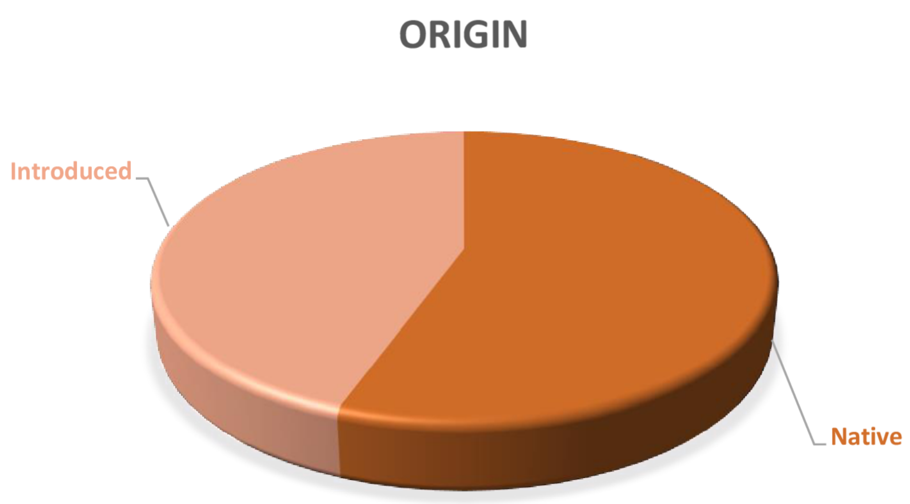

Figure 4. Chart displaying the origin of the 27 studied plants

Figure 5 illustrates the findings of the analysis on herbal recipes, revealing that infusion is the most prevalent preparation method, accounting for 71%. Following infusion, decoction is used at 8%, while juice, crushed fresh, cooked, and eaten raw constitute 6%, 6%, 3%, and 3% respectively. Additionally, Figure 6 shows the plant parts used in these processes. Notably, the leaf stands out as the most commonly used part at 37%, with the stem closely behind at 18%. Other plant parts include bark (11%), whole plant (10%), aerial part (8%), flower (5%), fruit (5%), root (3%), and seed (3%). Further insights are displayed in Table 1 which presents comprehensive details including scientific and local names, botanical families, preparation methods, plant parts used, habit, and origin of the studied species. Moreover, Figure 7 illustrates the distribution areas in Ecuador of the mentioned species.

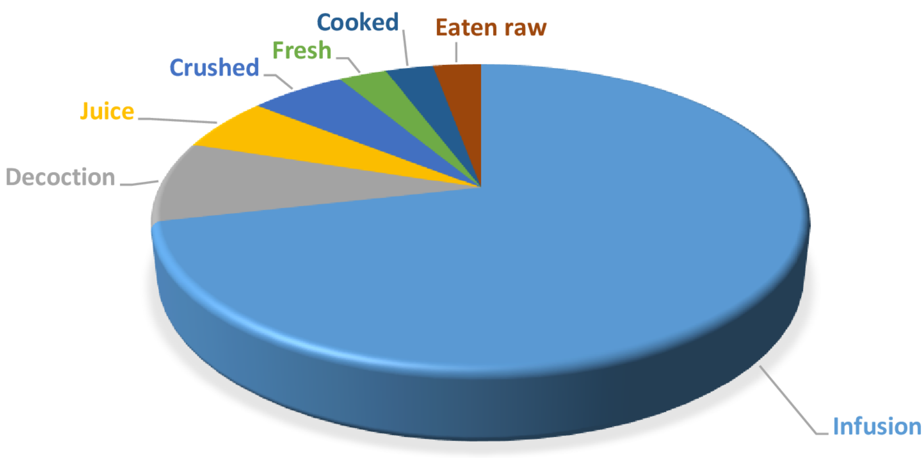

Figure 5. Graph of preparation methods

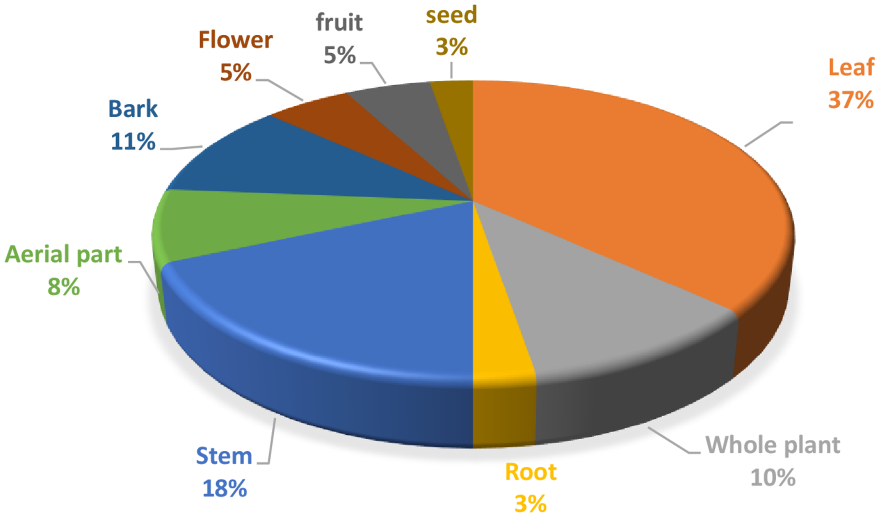

Figure 6. Graph of Plant part used

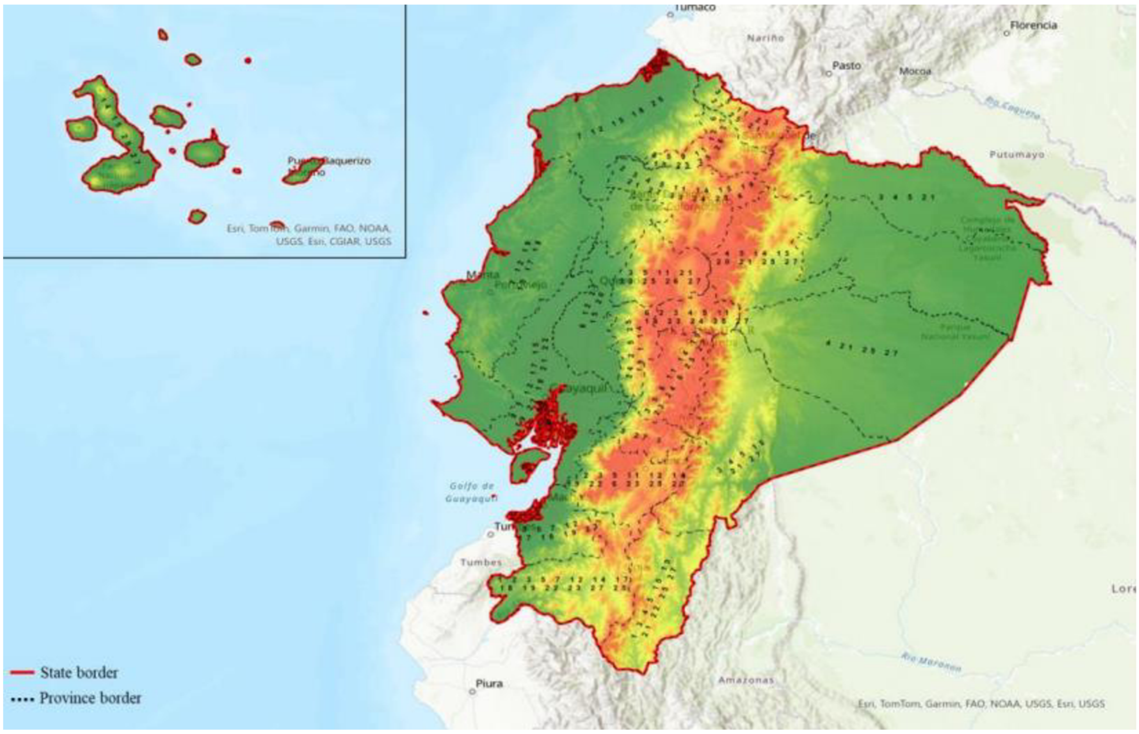

Figure 7. A simplified map showing the distribution of 27 medicinal plants with antidiabetic properties in Ecuador.1-*Justicia colorata* (Nees) Wassh, 2-*Foeniculum vulgare* Mill., 3-*Neonelsonia acuminata* (Benth.) J.M.Coult. & Rose ex Drude, 4-*Ilex guayusa* Loes., 5-*Baccharis genistelloides* (Lam.) Pers., 6-*Matricaria chamomilla* L., 7-*Ipomoea carnea* Jacq., 8-*Costus comosus* Roscoe, 9-*Costus villosissimus* Jacq., 10-*Bryophyllum gastonis-bonnieri* (Raym.-Hamet & H.Perrier) Lauz.-March.,

11-*Croton wagneri* Müll.Arg., 12-Cajanus cajan (L.) Millsp., 13-*Pelargonium graveolens* L'Hér., 14-*Juglans neotropica* Diels, 15-*Persea americana* Mill., 16-*Glycyrrhiza glabra* L., 17-*Myroxylon peruiferum* L.f., 18-*Pithecellobium excelsum* (Kunth) Mart., 19-*Siparuna eggersii* Hieron., 20-*Artocarpus altilis* (Parkinson) Fosberg, 21-*Piper crassinervium* Kunth, 22-*Oreocallis grandiflora* R.Br., 23-*Adiantum poiretii* Wikstr., 24-*Ruta graveolens* L., 25-*Physalis peruviana* L., 26-*Urtica dioica* L., 27-*Verbena litoralis* Kunth.

6. Literature findings about species clinical studies related to Diabetes treatment

Antidiabetic properties of 22 studied species (81%) from a total of 27 were scientifically confirmed, validating the appropriate usage of these species by traditional healers in Ecuador. No existing pharmacological studies have provided evidence supporting the antidiabetic activity of *Bryophyllum gastonis-bonnieri*, *Costus villosissimus*, *Juglans neotropica*, *Pithecellobium excelsum* and *Myroxylon peruiferum*. Plants were categorised into 23 botanical families, with the highest species representation observed in the *Asteraceae, Apiaceae, Costaceae*, and *Leguminosae* families, each containing two representative species. Additionally, 19 families included one species each. Used methods were most frequently α-glucosidase and α-amylase assay which were employed in 15 cases followed by models involving diabetes-induced rats with 8 cases. One different method was used in the case of *Physalis peruviana* where antidiabetic activity involved inducing diabetes in guinea pigs.

Adiantum poiretii Wikstr.

Adiantum poiretii, a perennial or rhizomatous geophyte belonging to family *Pteridaceae*, grows in the wet tropical biome. Its native range extends in Tropical & Subtropical America, Nigeria to Ethiopia and S. Africa, Arabian Peninsula, Indian Ocean, India, and Sri Lanka. Valued for its medicinal applications and environmental uses, this species serves various purposes in traditional medicine (POWO 2024).

The methanol extract from *Adiantum poiretii* was demonstrated to possess antidiabetic properties, revealing moderate inhibition activity against α-glucosidase, an enzyme responsible for reducing post-meal blood sugar spikes, with calculated IC_{50} values of 46.3 ± 0.92. However, no significant activity on α-amylase was observed in the study (Jaramillo Fierro & Ojeda Riascos 2018).

Artocarpus altilis (Parkinson) Fosberg

Artocarpus altilis, commonly referred to as breadfruit and classified under the *Moraceae* family, is recognized for its richness in carbohydrates. The genus *Artocarpus* is distributed in tropical and subtropical regions. Extracts and metabolites derived from various parts of the plant, including leaves, stems, fruits, and peels, harbour a number of biologically active compounds. These compounds exhibit diverse beneficial properties, contributing to antibacterial, antitubercular, antiviral, antifungal, antiplatelet, anti-arthritis, tyrosinase inhibition, cytotoxicity, and antidiabetic mellitus activities (Rante et al. 2019).

Significant enzyme inhibitory activity on α-glucosidase was indicated in ethanol extracts from breadfruit leaves which exhibited significant activity with stronger value in yellow leaves (IC_{50} values of 9.07 ppm) and lower in green leaves (11.01 ppm). The positive control, acarbose, demonstrated the strongest inhibitory activity with an IC_{50} of 6.79 ppm. Due to their inhibitory effects on α-glucosidase enzymes potential antidiabetic activity of breadfruit leaves is suggested (Rante et al. 2019).

Baccharis genistelloides (Lam.) Pers.

Baccharis genistelloides, identified as an herb or shrub within the Asteraceae family, is part of a genus consisting of over 400 species, with approximately 90% found in South America. Utilised for liver disorders and antipyretic purposes, *Baccharis genistelloides* is also employed for various diseases such as digestive disorders, malaria, diabetes, ulcers, sore throat, tonsillitis, anaemia, diarrhoea, indigestion, intestinal worms, and leprosy. *B. genistelloides* is widely used in traditional medicine, often prepared through infusion, attributed to its anti-inflammatory properties (Hennig et al. 2011).

Antidiabetic activity of *B. genistelloides* was analysed through inhibition assays where *Baccharis genistelloides* showed significant inhibitory activity against α-glucosidase enzymes, revealing an IC_{50} value of 154.6 ± 1.28 μg/mL. This discovery suggests a capability of *B. genistelloides* in modulating glucose metabolism and beckons further exploration within therapeutic contexts (Jaramillo Fierro & Ojeda Riascos 2018).

Cajanus cajan (L.) Millsp.

Cajanus cajan, locally known as Fréjol de palo, belonging to the Fabaceae family, is a perennial shrub indigenous to Asia, widely consumed as a pulse throughout the Asian subcontinent. Extracts or components derived from *Cajanus cajan* find extensive global use in treating conditions such as diabetes, dysentery, hepatitis, and measles, while also serving as a febrifuge to regulate menstrual periods. Notably, the leaves of *Cajanus cajan* are abundant in flavonoids and stilbenes, which are considered responsible for the beneficial effects on human health (Mosaddik et al. 2014).

Antidiabetic activity of *Cajanus cajan* and *Tamarindus indica* was compared in a study on alloxan-induced diabetic Swiss albino mice. Extract of each plant was orally administered in a dose of 200 and 400 mg/kg. *Cajanus cajan* showed higher potential in reduction of blood glucose levels with maximum reduction of 54.51% and IC_{50} 17.44 μg/mL. Results furthermore revealed high antioxidant capacity in both species (Mosaddik et al. 2014).

Costus comosus Roscoe

Costus comosus, a perennial plant native to Ecuador, belonging to the *Costaceae* family and commonly known as red tower ginger. In addition to the ornamental appearance, this rhizomatous plant holds a rich tradition of medicinal use. The leaves and rhizomes of *Costus comosus* have traditionally been employed for treating fever, rash, asthma, bronchitis, intestinal worms, diabetes, and liver diseases (Ramalingam. et al. 2021).

Antidiabetic properties of *Costus comosus* were studied based on their inhibition abilities on α-glucosidase and α-amylase enzymes. Extract from *C. comosus* showed activity only on α-glucosidase with IC_{50} value 57.9 ± 0.71 (Jaramillo Fierro & Ojeda Riascos 2018).

Croton wagneri Müll.Arg.

Croton wagneri, a member of the *Euphorbiaceae* family commonly referred to as moshquera blanca or moshquera, stands as an endemic and locally abundant shrub in the Andean region of Ecuador. This shrub is documented in at least seven populations extending from the Carchi province in the north to the Azuay province in the south (Pino et al. 2018). Utilising the moshquera plant in food preparations has the potential to elevate their nutritional composition (Portelles et al. 2020).

Enzymes, α-amylase (AAH) and α-glucosidase (AGH), inhibitory activity of *Croton wagneri* and other plants was investigated and later on compared based on their resulting IC_{50} values. O. grandiflora showed the best inhibitory activity with values AGH 2.8 ± 0.40 and AAH 161.5 ± 1.30. *C. wagneri* also demonstrated inhibition of α-amylase (IC_{50} > 1000) and α_glucosidase (IC_{50} = 162.4 ± 1.34) activity, although its effectiveness as an inhibitor was comparatively lower (Jaramillo Fierro & Ojeda Riascos 2018).

Foeniculum vulgare Mill.

Foeniculum vulgare, commonly known as fennel, stands as a widely recognized perennial herbaceous plant extensively employed in global herbal medicine and culinary practices. Belonging to the *Apiaceae* family, fennel has a rich history in ethnobotanical applications, addressing diverse health concerns such as gastrointestinal issues, hormonal disorders, and reproductive and respiratory diseases. Fennel provides flexible culinary choices, whether consumed raw, cooked, or baked (Jadid et al. 2023).

Antihyperglycemic effect of aqueous extract of *F. vulgare* (10 mg/kg) was demonstrated in a study on streptozotocin-induced diabetic (STZ) rats resulting in reduced blood glucose levels after 6 h from administration and without any loss of body weight. Furthermore, it improved oral glucose tolerance in diabetic rats. However, the extract's antioxidant ability was less efficient compared to a synthetic antioxidant, showing an inhibitory concentration (IC_{50}) for free radicals at 43±1.19 µg/ml, whereas the synthetic antioxidant BHT had an IC_{50} of 22.67±2.17µg/ml (El-Ouady et al. 2020).

Glycyrrhiza glabra L.

Glycyrrhiza glabra, a member of the *Leguminosae* family, holds a prominent position in the ancient medical traditions of Ayurveda, serving as both a medicinal herb and a flavouring agent. Commonly referred to as Licorice, Liquorice, or Sweet wood, *Glycyrrhiza glabra* is predominantly found in Mediterranean regions and specific areas of Asia (Kaur et al. 2013).

The effect of glycyrrhizin, extracted from *Glycyrrhiza glabra* root, was studied on streptozotocin-induced diabetic rats injected with glycyrrhizin (2.7 or 4.1 g/kg). Results showed improvement in modulating blood glucose level and confirmed the ability to lower blood insulin level (Al-Snafi 2018).

Ilex guayusa Loes.

Ilex guayusa, commonly referred to as Guayusa, is an underexplored holly species belonging to the only extant genus of the family *Aquifoliaceae*. Thriving in the upper Amazon basin across Colombia, Ecuador, and Peru, Guayusa holds cultural significance as societies in the region traditionally brew an infusion from its leaves for consumption (Dueñas 2016).

The hypoglycaemic and antioxidant activity of *Ilex guayusa* was studied in Ecuador, in which α-glucosidase and α-amylase inhibitory activities and the free radicals (DPPH, ABTS) of *I. guayusa* were explored. *I. guayusa* showed an IC_{50} value of 176.5 ± 1.50 μg/ml for α-glucosidase inhibition, indicating moderate inhibitory activity compared with *Oreocallis grandiflora*, with an IC_{50} value of 2.8 ± 0.40 μg/ml. Although *I. guayusa* showed less inhibitory activity against α-glucosidase, its high antioxidant potential suggests its possible importance in the treatment of diabetes due to its ability to counteract oxidative stress, a factor in the complications of diabetes (Jaramillo Fierro & Ojeda Riascos 2018).

Ipomoea carnea Jacq.

Ipomoea carnea, commonly known as Morning glory and a member of the *Convolvulaceae* family, is a shrub with a traditional application in folk medicine for managing diabetes and exhibiting muscle relaxant activity. It is recognized for their significant contribution as a natural source of antioxidants, particularly notable for their phenolic, flavonoid, and tannin content, showcasing their potential in therapeutic context (Khan et al. 2014).

The total phenolic, flavonoid and tannin content in different extracts of *I. carnea* leaves and its antidiabetic potential was investigated in streptozotocin induced diabetes Wistar rats that were injected with 500 mg/kg of *I. carnea* aqueous and alcoholic extract administered orally for three weeks. After three weeks of oral administration, both aqueous and alcoholic extracts showed a decrease in blood glucose levels, with the alcoholic extract demonstrating superior efficacy, although a reduction on body weight was noted (Khan et al. 2014).

Justicia colorata (Nees) Wassh.

Justicia colorata, locally known as Insulina, is a shrub indigenous to Ecuador and Peru, belonging to the Acanthaceae family. It grows in the wet tropical biome and is commonly prepared using the infusion method (POWO 2024).

Antidiabetic effect of *Justicia colorata* was confirmed in a study in Ecuador focusing on in vitro hypoglycaemic and antioxidant activities. Results show α-glucosidase inhibition activity with IC_{50} value 622.1 ± 2.52 (Jaramillo Fierro & Ojeda Riascos 2018).

Matricaria chamomilla L.

Chamomile (*Matricaria chamomilla*), a valued medicinal herb native to Europe, belonging to the *Asteraceae* family is often referred to as the "star among medicinal species." Its enduring significance is marked by widespread favour and extensive utilisation in folk and traditional medicine (Singh et al. 2011).

Antidiabetic activity of *Matricaria chamomilla* was studied in the aerial part of the ethanolic extract in streptozotocin-induced (STZ; 70 mg/kg) diabetic rats. Administration of varying doses of *M. chamomilla* led to a notable decrease in postprandial hyperglycaemia, oxidative stress and enhancement of the antioxidant system (Cemek et al. 2008).

Neonelsonia acuminata (Benth.) J.M.Coult. & Rose ex Drude

Neonelsonia acuminata, native to Mexico (Oaxaca, Chiapas), Venezuela and Peru, is a perennial herb within the *Apiaceae* family. Growing primarily in the subalpine or subarctic biome, its root is employed in traditional medicine, often consumed in its raw form (POWO 2024).

N. acuminata inhibitory effects on α-glucosidase and α-amylase, key enzymes in carbohydrate digestion, were analysed in a study. Results showed activity only on α-glucosidase with IC_{50} values of 198.7 ± 1.59 (1000 μg/mL), introducing an inhibitory capacity similar to established drugs used in diabetes treatment. Additionally, *Neonelsonia acuminata* displayed remarkable free radical scavenging activity (DPPH) 91±1.0 (100 μg/mL), indicating its prospective role as an alternative enzyme inhibitor and antioxidant in the management of diabetes mellitus (Jaramillo Fierro & Ojeda Riascos 2018).

Oreocallis grandiflora R.Br.

Oreocallis grandiflora, a species native to Ecuador within the *Proteaceae* family, is commonly known as cucharillo, cucharilla, gañal, and algil. Traditionally, its leaves and flowers, harvested during the blooming phase, are orally administered for the treatment of liver disease, vaginal bleeding, and inflammation of the ovaries and uterus. Additionally, it is employed as a remedy for digestive issues, diuretic effects, and hypoglycemic conditions (Vinueza et al. 2018).

A study performed in Ecuador tested antioxidant and antihyperglycemic activity in vitro of the extracts of *O. grandiflora*. This plant showed impressive ability in slowing down both α-amylase and α-glucosidase enzymes, with an IC_{50} value of 161.5 ± 1.30 μg/mL for α-amylase and an incredibly low IC_{50} value of 2.8 ± 0.40 μg/mL for α-glucosidase inhibition. These values signify its strong capability in inhibiting these enzymes, especially α-glucosidase, crucial for regulating blood sugar after meals. Moreover, its notable antioxidant activity suggests it could be valuable in combating oxidative stress, a significant factor in diabetes-related complications (Jaramillo Fierro & Ojeda Riascos 2018).

Pelargonium graveolens L'Hér.

Pelargonium graveolens, herb within the *Geraniaceae* family, is recognized for its aromatic properties. Its global cultivation primarily focuses on the extraction of essential oil employed mainly in the perfume industry due to its highly desirable scent (Ennaifer et al. 2018).

The antidiabetic potential of essential oil from *P. graveolens* was evaluated using an α-glucosidase inhibition assay. Findings showed that essential oil from *P. graveolens* (IC_{50} = 93.72±4.76) compared to acarbose (IC_{50} = 80.4±2.17) has similar efficiency in inhibiting α-glucosidase enzyme. Therefore, its efficiency in reducing post-meal blood sugar spikes was confirmed (Javed Ahamad & Subasini Uthirapathy 2021).

Persea americana L.

Avocado (*Persea americana*), a subtropical/tropical fruit from the *Lauraceae* family and native to Mexico, has gained significant popularity recently, often marketed as a "superfood" due to its distinct nutritional content, phytochemical composition, and associated health benefits. Beyond its culinary applications, it is traditionally used for various medicinal purposes such as blood pressure reduction, blood sugar control, antiviral properties, antidiarrheals, and cardiovascular disease (Abd Elkader et al. 2022).

The antidiabetic effects of *Persea americana* were confirmed in a study that evaluated the polyphenols content in ethanolic extracts of avocado fruit and leaves. According to the results obtained, the inhibition activity of α-amylase from fruit extract is higher (IC_{50} = 418) compared to avocado leaves (IC_{50} = 682) (Abd Elkader et al. 2022).

In another study the antidiabetic activity of avocado seeds was addressed. Performed in alloxan-induced diabetic male Wistar rats injected with aqueous extract of *Persea americana* seeds. Rats were separated into six groups and injected with different doses of the extract. Results exhibited maximal α-glucosidase inhibitory activity at 56.41% compared to acarbose, used as a reference drug, at 76.41%. The α-amylase inhibitory property shown in the aqueous extract was 21.42% compared to 76.41% for acarbose (Ojo et al. 2022).

Physalis peruviana L.

Physalis peruviana, a tropical herb within the *Solanaceae* family known as Golden berry or Cape gooseberry, is native to South America and cultivated in regions such as Egypt, India, and New Zealand. The fruits of Golden berry have a longstanding tradition in folk medicine, being utilised for the treatment of various conditions including diabetes, hepatitis, malaria, dermatitis, asthma, and rheumatism (Ezzat et al. 2021).

Antidiabetic activity was tested on guinea-pigs injected with aqueous extract from dried leaf powder of *Physalis peruviana*, ranging from 100 mg/kg to 3.2 g/kg of body weight. To evaluate the ability to lower blood sugar, a glucose tolerance test was conducted by feeding the animals 4 g/kg of glucose and measuring blood sugar levels at different intervals. *Physalis peruviana* showed a notable decrease in blood sugar levels at a dose of 100 mg/kg. However, higher doses caused intoxication (Kasali et al. 2013).

Piper crassinervium Kunth

Piper crassinervium, known as Guabiduca in Ecuador, is a shrub in the *Piperaceae* family found throughout South America. Its significance in traditional medicine and potential for essential oil production makes it suitable for commercial use (Gomes & Krinski 2018).

It was confirmed that extract from *Piper crassinervium* effectively slows glucose absorption and suppresses postprandial hyperglycemia. The results revealed the ability to inhibit the α-glucosidase enzyme therefore helping to break down complex sugars into simpler sugars such as glucose (Jaramillo Fierro & Ojeda Riascos 2018).

Ruta graveolens L.

Ruta graveolens, commonly known as Rue and belonging to the *Rutaceae* family, is a subshrub native to the Mediterranean region and now cultivated globally. Rue has been a significant component of European pharmacopoeia since ancient times. Extracts and essential oil derived from *R. graveolens* play an important role in drug development, exhibiting various pharmacological activities. Traditionally, R. graveolens has been used in traditional medicine for relieving pain, addressing eye problems, managing rheumatism, and treating dermatitis. Recent research confirmed its antibacterial, analgesic, anti-inflammatory, antidiabetic, and insecticidal properties (Asgarpanah & Roghaieh 2012).

Antidiabetic properties of *Ruta graveolens* were studied using α-glucosidase and α-amylase inhibition assay. Chloroform and methanol extract was prepared from 20 grams of plant powder and furthermore studied. Findings revealed that methanolic extract showed higher inhibitory activity of α-glucosidase and α-amylase with an IC_{50} value of 281 and 215 µg/mL, showing better activity than the reference drug acarbose. (Ardeshirlarijani et al. 2019).

Siparuna eggersii Hieron.

Siparuna eggersii, a shrub belonging to the *Monimiaceae* family, is endemic to the Loja province in Ecuador, locally known as "monte del oso." It has a high ethnic value in equatorial regions but this species is currently facing the threat of extinction (Ruiz et al. 2010).

The inhibitory activity of *Siparuna eggersii* on α-glucosidase and α-amylase was investigated in a study in which results demonstrated notable inhibitory activity against α-glucosidase enzymes, revealing an IC_{50} value of 28.3 ± 0.60 µg/mL. This finding suggests a compelling potential of *S. eggersii* in a diabetes treatment (Jaramillo Fierro & Ojeda Riascos 2018).

Urtica dioica L.

Urtica dioica L., commonly known as nettle, is a perennial flowering plant originating from Europe, temperate Asia, and western North Africa, with widespread cultivation across the globe (Tatke & Waghmare 2024). As a member of the Urticaceae family, nettle is recognized for its valuable bioactive compounds, including formic acid and abundant flavonoids, making it an important subject in phytotherapy. Utilised in various forms such as crude dried powder, infusion, dry extract, decoction, or fresh juice, nettle has been extensively studied. Numerous studies highlight the therapeutic potential of *U. dioica*, demonstrating its effectiveness in addressing various disorders such as prostatic hyperplasia, rheumatoid arthritis, allergies, anaemia, internal bleeding, kidney stones, and burns. Additionally, it shows anti-proliferative and antimicrobial activities, demonstrating efficacy in the treatment of infectious diseases (Samakar et al. 2022).

Antihyperglycemic activity of the aqueous extract of *Urtica dioica* (250 mg/kg) was demonstrated in a study with Male Wistar rats and Swiss mice of both sexes that were administrated with 250 mg/kg of *U. dioica* and with glucose (1 g/kg) 30 minutes later. The results indicate a decrease in glycaemia approximately 33% vs. control in the first hour after glucose insertion. Furthermore, the reduction of intestinal glucose absorption was observed (Bnouham et al. 2003).

Verbena litoralis Kunth

Verbena litoralis, a member of the *Verbenaceae* family, is a native South American herb with a history in traditional medicine. In South and Central America, it has been traditionally used for addressing conditions such as diarrhoea, fever, gastrointestinal disorders, and certain sexually transmitted diseases. This plant attracted more attention for its nerve growth factor-potentiating activity (Braga et al. 2012).

A study elucidated the inhibitory activity on α-glucosidase and α-amylase, the key enzymes responsible for breaking down sugars. Extract from *Verbena litoralis* showed inhibitory activity on α-glucosidase with IC_{50} values 337.9 ± 1.75 and was non active in α-amylase inhibition (Jaramillo Fierro & Ojeda Riascos 2018).

7. Conclusions

The present review demonstrates a great diversity of plant species used in traditional medicine of Ecuador for treatment of Diabetes. It identified 27 species with potential antidiabetic properties, and their effectiveness was scientifically confirmed in 22 cases. The verification of antidiabetic activity employed methods such as α-glucosidase and α-amylase assays, along with models utilising rats and guinea pigs induced with diabetes. This information confirms the appropriate use of traditional medicine in Ecuador. However, additional ethnobotanical studies, pharmacological analyses, and human trials are essential for deeper knowledge.

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