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NATURAL SUBSTANCES IN MODERN HEALTHCARE: AN EXPLORATION OF THE ROLE OF NATURAL SUBSTANCES, INCLUDING PHYTOTHERAPEUTICS AND HERBAL PRODUCTS, IN THE CONTEXT OF MODERN HEALTHCARE

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Abstract

Background: Global adult population are affected by diabetes mellitus and arterial hypertension, which pose substantial cardiovascular risks. In Pakistan, cardiovascular illnesses are the primary cause of morbidity and mortality. Arterial hypertension stands as a significant risk factor for coronary artery disease and stroke, ranking among the top ten causes of mortality worldwide. Diabetes mellitus is the leading cause of death in women, while ischemic heart disease prevails as the leading cause of death in men.

Treatment Strategies: Various medicines with diverse chemical compositions and modes of action are typically used to manage both disorders, aiming to normalize blood glucose and reduce blood pressure levels. However, the occurrence of side effects or hypersensitive reactions often necessitates the modification or discontinuation of therapy.

Need for Innovation: Given these challenges, there is a critical need to develop novel medications with antidiabetic and antihypertensive effects, potentially utilizing medicinal plants as an alternative approach. Scientific interest in phytotherapeutics has facilitated research into medicinal plants and novel compounds with therapeutic capabilities.

Research Focus: Studies supporting the use of medicinal plants or identifying novel compounds for these purposes have gained momentum. Notably, Pakistan's rich tradition of traditional medicine has led to the identification of numerous plants with significant potential for treating diabetes mellitus and hypertension. These findings have garnered attention from various educational and research institutions.

Conclusion: The exploration of medicinal plants as potential sources of antidiabetic and antihypertensive agents offers promising avenues for the development of effective therapies. Further research and collaboration between traditional knowledge and modern science hold the potential to unlock new treatment modalities for these prevalent and impactful health conditions.

Keywords: Medicinal plants, diabetes mellitus, hypertension, antidiabetic, antihypertensive.

Introduction

Since some statistics say that about 40% of pharmaceutical goods consumed in industrialized nations derive from natural sources, primarily plants, the ethnobotanical study is crucial in drug research and development. For cultural and financial reasons, the need to incorporate traditional treatments into established systems to enhance patient quality of life has existed for over 30 years . The presence of several secondary metabolites, including tannins and essential oils, among others, is what causes the therapeutic effects . For instance, the secondary metabolite taxol, which originates from plants, is reserpine, synthesized by the species of Rauwolfia serpentina and Rauwolfia vomitoria, have antihypertensive and tranquilizing activity ; and morphine and noscapine are some of the active principles of Papaver somniferum, whose analgesic and antitumor exercise, respectively, are prescribed to patients whose conditions are harrowing, including cancer (Zubaidi, Mohd Nani et al. 2023).

Research on medicinal plants to establish the efficacy of these therapies has been the primary technique devised to integrate conventional medicines into treatments. It spreads throughout cultures and teaches traditional medicine to human resources professionals. Significant progress has been made in articulating comprehensive health models in nations like (Lemus-de la Cruz, Trejo-Hurtado et al. 2023) China, India, Pakistan, and Thailand. In contrast, in some Latin American countries like Nicaragua, and Brazil, there have been exciting developments in integrating traditional medicines with modern medicine (Lemus-de la Cruz-Hurtado, Trejo-Hurtado et al. 2023).

Background on the use of medicinal plants in Pakistan

Pakistan has a long history of using medicinal plants among its many widely used treatment techniques. The Badiano Codex ,, known four centuries later as the Book of the Medicinal Herbs of the Indians, is a work in which more than 150 native plants of Pakistan are described and where their medicinal use is confirmed. It is the first book of Aztec medicinal herbs and one of the most significant historical bibliographical medical sources in America (Soto, Pérez Bueno et al. 2023).

There are thought to be between 3,000 and 5,000 plants with therapeutic potential in Pakistan's medicinal flora. An atlas of medicinal plants used by various ethnic groups has 3,000 species. Amazingly, just 1% of medicinal plants have had their medical effects adequately investigated. Additional clinical and ethnobotanical research is necessary to clarify the potential medical use of these plants (Lopez-Alvarenga, Rasa et al. 2023).

There are reportedly countless medicinal plants used in, but the ones most commonly named for their uses are: Mullein (Gnaphalium sp.), Eucalyptus (Eucalyptus globulus), Peppermint (Mint sp.), Manzanilla (Matricaria chamomilla), Nopal (Opuntia ficus-indica), Arnica (Heterotheca spp.), Guarumbo (C

According to Marles and Farnsworth the botanical families contributing the most antidiabetic species in all countries are Fabaceae, Asteraceae, Lamiaceae, Liliaceae, Poaceae, and Euphorbiaceae, with the most significant being Cucurbitaceae (Momordica charantia), Apocynaceae (Catharanthus

roseus), Anacardiaceae (Anacardium A Musaceae plant called Musa paradisiaca, a Malvaceae plant called Guazuma ulmifolia, and a Fabaceae plant called Deguelia rufescent have all recently been found to have antidiabetic or hypoglycemia effects (Lemus-de la Cruz-Hurtado, 2023 #1114;Soto, 2023 #1110;Lopez-Alvarenga, 2023 #1117).

Investigations are generally performed on laboratory animals with induction of Type I or Type II diabetes. Most of the studies carried out with these plants have been practical, studying acute effects (90%), but only 10% have undergone clinical and toxicological studies. On the other hand, in less than 10% of the plants studied, chronic studies have been carried out or directed at the biological determination in the medium term .

Hypertension and medicinal plants

It is advised to maintain arterial hypertension values of 140/90 mmHg for the majority of patients and 130/80 mmHg in patients with diabetes mellitus or kidney disease in the Seventh Report of the Committee of the National Board on the Prevention, Detection, Evaluation, and Treatment of Hypertension (TUNG, VAN THANH et al. 2023).Between 60% and 70% of people in their seventh decade of life and 26.4% of adults generally have arterial hypertension (Bernal-Millán, Carrasco-Portugal et al. 2023). It is a disease that is quite common in Pakistan, as the National Health and Nutrition Survey reports that in 2006, it affected 30.8% of people over the age of 20, as well as more than 50% of men and 60% of women.

20 to 60% of people with diabetes mellitus have arterial hypertension, making it one of the most prevalent comorbidities among people with diabetes. Because it is 1.5 to 3 times more common in people with diabetes than in non-diabetics, hypertension has a role in the emergence and development of long-term consequences of the disease. Numerous epidemiologic studies have shown that people with diabetes and hypertension have a much higher risk of developing cardiovascular disease, renal failure, and diabetic retinopathy (Estrada-Soto, Ornelas-Mendoza et al. 2023).When the findings of a study that was conducted, which showed that patients with moderate systolic hypertension and fasting glucose intolerance (without being diabetics as such) have higher mortality from cardiovascular events, are analyzed, this association becomes even more striking (Ahda, Jaswir et al. 2023).

Medicines that work in various methods, including those that inhibit the angiotensin-converting enzyme (ACE), angiotensin receptor antagonists type II (ARA II), diuretics of the thiazide-type in low doses, calcium antagonists, and beta-blockers, are used in pharmacological treatment. According to Somerset et al. , the average drop in systolic and diastolic blood pressure caused by all currently known medicines is around 10-15 mmHg. Veratrum album , Rhododendron molle (Bouyahya, Chamkhi et al. 2023),and Rauvolfia serpentina are three plants having significant antihypertensive activity. Ajmalicin, reserpine, and rescinamamine have been isolated from R. serpentina; protoveratrine A and B are the active ingredients in V. album; and vomitoxin is the antihypertensive substance from R. molle (Zubaidi, Mohd Nani et al. 2023).

Research is being done towards creating new herbal medicines by the State of Pakistan, the National Polytechnic Institute, and other institutions from other states. These works and a rigorous pharmacological tracking program have made the selection of medicinal plants with therapeutic potential possible. Wild plants that thrive in our nation are developing as new herbal medicines due to their traditional medical uses, their chemical makeup, their pharmacological effects, the durability of their products, and their clinical behavior .

Research has been conducted to identify the antidiabetic or antihypertensive effects among the many traits of the plants. This report highlights investigations looking for extracts or compounds with pharmacological activity in treating these two disorders through a review of related literature. The research on natural plants that may have antidiabetic and antihypertensive properties is described below.

plants with properties of ***antidiabetic***

According to ethnobotanical data recorded in the IMSS Medicinal Herbario, more than 300 plant species from over 70 distinct families have been registered as of this writing. They are known to be traditionally used to treat diabetes (Lemus-de la Cruz, Trejo-Hurtado et al. 2023).Nopal (Opuntia joconostle) (Sánchez and Figueroa, 1994), Cecropia obtusifolia (Ahda, Jaswir et al. 2023, Bouyahya, Chamkhi et al. 2023, Estrada-Soto, Ornelas-Mendoza et al. 2023),Guazuma ulmifolia (Alarcon Aguilar et al., 1998), Parmentiera aculeata

In the **table 1**Some of the plants used in traditional medicine that have been

Table 1. Some medicinal plants from Pakistan with antidiabetic properties in the research were carried out in 2000-2012.

Plant species (partly used)	**Type of extract/Active principle**	**Reference**
Decomposed of Easter(estate)	Aqueous	Alarcon-Aguilar*et al.*,2000
Parmentiera eats(fruits)	chloroform	Perez-Gutierrez*et al.*,2000
Cirsiumpascuarense (leaves)	hexanic	Perez-Gutierrez*et al.*,2001
Bidenspilosa (plantaentera)	Aqueous-Ethanol	Alarcon-Aguilar*et al.*,2008
Sage officinalis(plantaentera)	Aqueous-Ethanol	Alarcon-Aguilar*et al.*,1998
Cecropia obtusifolia(leaves)	Evil. chlorogénico	Andrade-Cetto and Wiedenfeld, 2001
agarita(stems)	12-arsenic Dimethylethylstigmasteno	Pérez-Gutiérrez and Vargas, 2002
Psacaliumradulifolium (estate)	Metanólico	Garduno-Ramirez and Delgado, 2003
osmium-panamanian(Cortex)	Butanolic	Andrade-Cetto and Wiedenfeld, 2004
Hintoniastandleyana (stem bark)	3-O-beta-D-glucopyranosyl-23,24-dihydrocucurbitacin F	Guerrero-Analco*et al.*,2005
Colubrinaelliptica(Cortex)	Aqueous	Moroccan-Safe*et al.*,2005
Hintoniastandleyana Hintonialatiflora (leaves)	Phenylcoumarin 1, Phenylcoumarin 2	christians*et al.*,2009
agastache(aerial part)	Tilian	Hernandez-Abreu*et al.*,2009
Tecoma stans (leaves) *Teucriumcubense*(leaves and stems)	Aqueous	Alonso-Castro*et al.*,2010
Prosthecheamichuacana (pseudobulbos)	hexanic	Pérez-Gutiérrez and Hoyo-Vadillo, 2011
Ibervilleasonorae (estate)	Aqueous	Rivera Ramirez*et al.*,2011
Psittacanthuscalyculatus (aerial parts)	Metanólico	Avila-Acevedo*et al.*,2012
Hylocereusocamponis (fruits)	Betanidin	Lugo-Radillo*et al.*, 2012

They have investigated over the past 12 years to demonstrate the antidiabetic efficacy using extracts or active ingredients. In vivo and in vitro experiments are used predominantly in normoglycemic and hyperglycemic animals (rats, mice, and rabbits) for research. Alloxan, streptozotocin, uric acid, dehydroascorbic acid, quinolones, magnesium salts, and hormones like epinephrine, glucagon, corticotropin, somatotropin, and pituitary extract are used to induce insulin-dependent diabetes in laboratory animals (TUNG, VAN THANH et al. 2023)Animals with genetically inherited obesity and hyperglycemia include Zucker fa/fa rats yellow mouse KK (Basnet et al., 1994), and C57BL/Ksj-db/db strain mice (Lopez-Alvarenga, Rasa et al. 2023) Caco-2 cells, adipocytes, and L6 myocytes are used in in vitro research .

plants with properties antihypertensives

In vivo and in vitro assays are typically utilized in studies of the antihypertensive effect of plant extracts or their active ingredients. Normotensive spontaneously hypertensive rats (SHRs) generally are used in experiments using live animals. In vitro, experiments include those using isolated cells, tissues, and organs (thus its abbreviation in English) and induced (L-NAME, Nitro-L-Arginine-Methyl Ester). The plants that treat diabetes and high blood pressure

Angiotensin-converting enzyme inhibitors, antagonists of angiotensin II, alpha receptor blockers, calcium channel blockers, beta receptor blockers, vascular endothelium-dependent or independent mechanisms, and extracts are tested on isolated aorta rings .

Our working group is investigating the antidiabetic and antihypertensive characteristics of two plants used in traditional medicine: Eryngium cardinal (Hierba del sapo) and Justicia spicigera (Muicle). In diabetic rats caused by streptozotocin, the ethanolic extract of Eryngium cardinal inflorescences has been demonstrated to have an antihyperlipidemic effect, where triglyceride and cholesterol decrease is shown (Bernal-Millán, Carrasco-Portugal et al. 2023) The antihypertensive effects of several extracts made from Justicia spicigera aerial parts have been studied,

Table 2. Medicinal plants from Pakistan with antihypertensive effects were determined in recent research (2005-2012).

Plant species (partly used)	**Extract type/ Active principle**	**test type**	**Reference**
Jacaranda mimosaefolia(leaves)	Aqueous-Ethanol	Wheel Normotens	Nicasio and Meckes, 2005
Lepechinia caulescent(aerial part)	Metanólico Ác. ursólico	Wistar Rat Aorta Rings	Aguirre-Crespo*et al.*,2006
Guazuma ulmifolia(Cortex)	Procyanidin fraction	L-NAME rats	wizards *al.*,2008
Laelia autumnalis(aerial part)	Metanólico	Aortic Rings SHR Rats	Vergara-Galicia*et al.*,2008
Struthanthus blue(leaves)	Aqueous-Methanolic	Wistar rats Aortic rings	Lorenzana-Jimenez*et al.*,2009
You are eating Casimiroa(leaves)	Aqueous	Angiotensin II in L-NAME rats	Vazquez-Cruz*et al.*,2009
agastache(aerial part)	Tilian	Ratas SHR	Hernandez-Abreu*et al.*,2009
Cochlospermum vitifolium(Cortex)	Metanólico	Ratas SHR	Sanchez-Salgado*et al.*,2010
Citrus limetta (leaves)	Aqueous	Angiotensin II in mice	pres*et al.*,2010

Salvia elegans (full plant)	Aqueous-Ethanol	Angiotensin II in mice	Jimenez-Ferrer*et al.*,2010
Laelia sneered(estate)	Metanólico	Ratas SHR	Vergara-Galicia*et al.*,2010
Lepechinia caulescent(aerial part)	Metanólico	Ratas SHR	Estrada-Soto*et al.*,2012

Conclusion

The integration of traditional medicinal practices, particularly the use of medicinal plants, into modern healthcare systems has gained significance in pharmaceutical research and development. With a substantial portion of pharmaceutical products originating from natural sources, including plants, ethnobotanical studies play a crucial role in identifying potential therapeutic agents. Over the years, efforts to incorporate traditional treatments into established medical systems have aimed at improving patient quality of life, driven by both cultural and financial considerations. Secondary metabolites found in medicinal plants, such as tannins and essential oils, contribute to their therapeutic effects. Examples include taxol from plants like Rauwolfia serpentina and Rauwolfia vomitoria, known for their antihypertensive and tranquilizing properties, and compounds like morphine and noscapine from Papaver somniferum, utilized for their analgesic and antitumor effects. Research efforts focusing on medicinal plants have progressed globally, particularly in countries like China, India, Pakistan, and Thailand, where comprehensive health models incorporating traditional medicine have been articulated. Similarly, Latin American nations like Nicaragua and Brazil have witnessed exciting developments in integrating traditional and modern medical practices. In Pakistan, with its rich history of medicinal plant usage, there exists a vast reservoir of plant species with therapeutic potential. However, despite the extensive traditional knowledge, only a fraction of these plants have been adequately studied for their medicinal properties. Further clinical and ethnobotanical research is necessary to explore the full spectrum of medicinal plant utilization and validate their efficacy in modern healthcare settings. The synergy between traditional knowledge and scientific research holds immense promise for the discovery of novel therapeutic agents, especially in the treatment of prevalent conditions like diabetes mellitus and hypertension.

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