

Chapter 1: Introduction and Objectives

1.1 Introduction

Since ancient times, medicinal plants have been utilized as an integral part of healthcare, offering a compelling alternative to synthetic drugs. Approximately 80% of the population in developing countries utilized plant-based remedies for primary healthcare (Sofowora et al., 2013). It highlights the significance of ethnopharmacological research, which focuses on evaluating the efficacy, safety, and potential for drug discovery from traditional medicinal practices (Süntar, 2020). Plants have played a central role in traditional healthcare systems, especially among tribal communities, which have accumulated extensive knowledge about the use of plants and plant products as herbal remedies (Uniyal et al., 2006). The ancient religious scripture "Rigveda," written between 4000 and 1600 B.C., documents the utilization of the plant "Soma" as a medicinal agent by the Indo-Aryans (Saleem et al., 2013). Such traditional knowledge serves as a valuable resource for scientific exploration and research, validating the claims of these ancient practices.

Ethnomedicinal plants have attracted significant global attention from scientists and researchers, spanning various disciplines such as pharmacology, phytochemistry, and clinical studies. According to estimates, between 35,000 and 70,000 plant species are utilized globally for cosmetic, nutraceutical, and medical uses (Vasisht et al., 2016). Globally, the demand for herbal products is rising quickly, and large pharmaceutical firms have investigated medicinal plants for possible medical uses.

Ayurveda, one of the traditional systems of medicine in India, is recognized by the WHO and has been practised for over 5,000 years (Mukherjee and Wahile, 2006). Ayurveda utilizes approximately 80% plant-based substances, 12% animal-based substances, and 8% mineral-based products for curing diseases (Chunarkar-Patil et al., 2024; Jaiswal et

al., 2016). Today, about one-fourth of the drugs are plant-based, and 121 reported active compounds derived from plants are currently in use (Qadir and Raja, 2021). Out of 252 drugs listed by WHO, 11% are derived from plants (Al-Harrasi et al., 2022). In many African and Asian countries, nearly 80% of the population depends on traditional remedies for their primary medical care (Mahomoodally, 2013).

Approximately 80% of people living in rural areas of India use traditional medical systems or medicinal herbs (Muthu et al., 2006). The Indian herbal industry utilizes around 960 plant species, with 178 species in high demand, each exceeding 100 metric tonnes annually. India has one of the most diversified groups of medicinal plants in the world, due to its vast biodiversity and cultural legacy (Sen et al., 2011). India is blessed with various traditional medical systems, including Unani, Ayurveda, Siddha, and Homeopathy. India is considered one of the 12 mega-biodiverse countries globally, with significant plant biodiversity concentrated in hotspots like the Eastern Himalayas, Northeast India, the Western Ghats, and the Andaman and Nicobar Islands (Patra and Basu, 2021).

Among these medicinal plants, *Hemidesmus indicus* (Indian Sarsaparilla) and *Ichnocarpus frutescens* (Black Creeper) are two plants that have several therapeutic properties (Mary and Sukumar, 2024; Mueed et al., 2023). Both plants belong to the Apocynaceae family and are native to the Indian subcontinent, where they have been used extensively in Ayurveda and other traditional medicinal practices (Kumar and Gairola, 2020; Mohsina et al., 2022). These plants share common characteristics, including their use in treating ailments such as skin diseases, respiratory disorders, and inflammatory conditions. Their therapeutic properties are due to the presence of numerous bioactive constituents such as flavonoids, saponins, tannins, and alkaloids (Kumarappan et al., 2015a; Rajput, 2022)

Hemidesmus indicus, commonly known as Shwet Sariva, is a perennial shrub characterized by its woody rootstock and distinctive camphoraceous fragrance (Manjulatha et al., 2014). It is widely distributed across the Indian subcontinent, especially in regions like the upper Gangetic plain, West Bengal, Assam, and parts of central, western, and southern India (Nandy et al., 2020a). The plant is known for its extensive root system, often referred to as "Anantmool," meaning "the eternal root" (Chakraborty and Choudhary, 2014). In traditional medicine, particularly Ayurveda, Siddha, and Unani systems, root, stem and leaves of *Hemidesmus indicus* is used to treat skin disorders, respiratory problems, and digestive issues and as a general health tonic to enhance overall well-being (Kawlani et al., 2017). The therapeutic effects of *Hemidesmus indicus* are largely attributed to its rich content of saponins, flavonoids, and tannins, which contribute to its antimicrobial, anticancer, and antidiabetic potential (Sai et al., 2024).

Ichnocarpus frutescens, known as Krishna Sariva, is a red woody climber also belonging to the Apocynaceae family. It is highly regarded in traditional medicine for its diverse therapeutic applications (Mohsina et al., 2022). *Ichnocarpus frutescens* has been used by indigenous communities for treating various ailments, including fever, diabetes, skin diseases, and respiratory conditions (Kumarappan et al., 2015a). Its leaves, stems, and roots are utilized in different medicinal preparations, such as decoctions, infusions, and powders, reflecting its versatility in traditional healing practices (Rajput, 2022).

This research has explored the pharmacological potential of *Hemidesmus indicus* and *Ichnocarpus frutescens*, focusing on their possible roles in managing diabetes, oxidative stress, and cancer. Diabetes is a condition of high blood sugar that is caused by insulin enzyme deficiency in either its secretion, action, or both (Goldstein, 2002; Rachdaoui, 2020). Given the limitations of current antidiabetic treatments and the growing prevalence

of diabetes, there is an urgent need to discover new therapeutic agents. Both *Hemidesmus indicus* and *Ichnocarpus frutescens* have shown promising antidiabetic activity such as increasing insulin production, boosting glucose absorption, and inhibiting keys like α -A and α -G (a carbohydrate-digesting enzyme) (Kumari et al., 2023c; Nair et al., 2014; Taidala et al., 2024).

Oxidative stress, which is a mis-synchronization in antioxidant defence mechanism and reactive oxygen species or RoS, is a primary cause of chronic diseases including diabetes and cancer (García-Sánchez et al., 2020). Antioxidants play a crucial role in neutralizing ROS and preventing cellular damage (Rao et al., 2011). Both plants are rich in antioxidant compounds, which could help in mitigating oxidative stress-related diseases. Studies have shown that these plants possess significant antioxidant properties, making them valuable in protecting against oxidative damage and maintaining cellular health (Taidala et al., 2024; Tan et al., 2019).

Cancer, a leading cause of death globally, is characterized by uncontrolled cell growth and the potential to spread throughout the body (Singh and Roghini, 2023). Despite advancements in cancer treatment, searching for more effective and less toxic therapeutic agents remains a priority (Ma et al., 2016). Plant-based compounds offer a promising avenue for developing new anticancer drugs due to their diverse bioactive components (Shrihastini et al., 2021). Preliminary studies suggest that *Hemidesmus indicus* and *Ichnocarpus frutescens* have anti-cancer properties (da Silva et al., 2023; Kumarappan et al., 2009; Kumarappan and Mandal, 2007; Sena et al., 2023). These findings underscore the potential of these plants as sources of novel anticancer agents.

Despite their widespread use in traditional medicine, the precise mechanisms of action and therapeutic efficacy of *Hemidesmus indicus* and *Ichnocarpus frutescens* remain

underexplored. There is a growing interest in scientifically validating the traditional uses of these plants and understanding the molecular mechanisms underlying their health benefits. Comprehensive research on these plants contributes insightful information into their potential therapeutic applications, leading to the development of new treatments for diabetes, oxidative stress, and cancer.

1.2 Objectives

The primary objective of this research is to explore and validate the antidiabetic, antioxidant, and anticancer potential of *Hemidesmus indicus* and *Ichnocarpus frutescens*. The main goal of this study was to address the current research gaps about the bioactive chemicals found in these plants and their potential medicinal benefits. The specific objectives are as follows:

1. Extraction, Purification and Characterization of Bioactive constituents from *Hemidesmus indicus* and *Ichnocarpus frutescens*.
2. Evaluation of the antioxidant capacity of the *Hemidesmus indicus* and *Ichnocarpus frutescens* extracts and their phytoconstituents.
3. Biological evaluation and computational studies of isolated compounds as Antidiabetic potential: -
 - A. *In vitro* assays targeting key enzymes involved in glucose metabolism, such as α -Amylase and α -Glucosidase, as well as glucose uptake assays and wound healing assays.
 - B. Computational methods to predict the interaction of isolated compounds with α -Amylase and α -Glucosidase targets.
4. Biological evaluation and computational studies of the plant extracts and isolated compounds as anti-cancer potential.

5. Synthesis of zinc oxide nanoparticles using *Hemidesmus indicus* and *Ichnocarpus frutescens* root extract and their therapeutic applications.

To achieve these objectives, the study aims to provide a scientific basis and molecular mechanism for the traditional use of *Hemidesmus indicus* and *Ichnocarpus frutescens*, identify new bioactive compounds, and contribute to the development of novel natural therapies for diabetes, oxidative stress-related conditions, and cancer.