INTRODUCTION

Human inquisitiveness has extended too many corners of the Earth, to our solar system, and to the distant great clouds of nebulae which appear to be forming and reforming billions of suns and their solar systems. Inherent in the very existence of humankind has been the incessant desire to expand the boundaries of our knowledge and creativity, and thus a new vision of how life might continuously be improved on a global basis. For many humans, access to travel, to television, and to electronic communication has allowed, indeed encourage us, to engage with the breadth and depth of human and biological experiences across national boundaries and up and down the global ecochasms. The treasures now available from delving into these rich stores of biological and mineral wealth are amazing\(^1\).

Natural products, including plants, animals and minerals have been the basis of treatment of human diseases. History of medicine dates back practically to the existence of human civilization. The current accepted modern medicine of Allopathy has gradually developed over the years by scientific and observational efforts of scientists. However, the basis of its development remains rooted in traditional medicine and therapies. The history of medicine includes many ludicrous therapies. Nevertheless, ancient wisdom has been the basis of modern medicine and will remain as an important source of future medicine and therapeutics\(^2\).

The World Health Organization (WHO) has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been existence, often for hundreds of years, before the development and spread of modern medicine and
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are still in use today\(^3\). Traditional medicine is the synthesis of therapeutic experience of generations of practicing physicians of indigenous system of medicine. Indeed, more than 90% of current therapeutic classes derive from a natural product prototype and interestingly, even today, roughly two-thirds to three-quarters of the world’s population relies upon medicinal plants for its primary pharmaceutical care. Those “medicinal plants” are either preparations of or natural product substances from plants that have potential utility as pharmaceutical agents\(^4\).

Herbal drugs continue only those traditional medicines which primarily use medicinal plant preparation for therapy. The earliest recorded evidence of their use in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years. The classical Indian texts include Rigveda, Atherveda, Charaka Samhita and Sushrutha Samhita. The herbal medicines/traditional medicaments have, therefore, been derived from rich traditions of ancient civilizations and scientific heritage\(^5,6\). Herbal medicine is still the mainstay of about 75-80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, the last few years have seen a major increase in their use in the developed world\(^5\).

The conventional medicine is now beginning to accept the use of botanicals once they scientifically validated. *Ispaghula, Garlic, Ginseng, Ginger, Ginkgo, St.John’s Wort* and *Saw palmetto* are a few examples of botanicals which are gaining popularity amongst modern physicians. Similarly, studies on medicinal plants particularly on the biological aspects and the impact factor of the journals publishing such research are growing with rapid race. One can imagine the popularity of herbal medicine in the West from the fact
that an American Journal of Chinese Medicine exists in the literature. There is an increasing trend in the North America and Europe to incorporate the Complimentary and Alternative Medicine, particularly the herbs as an essential component in the medicine curriculum\textsuperscript{6}. In Germany and France, many herbs and herbal extracts are uses as prescription drugs and their sales in the countries of European Union were around $6 billion in 1991 and may be over $20 billion now. In USA, herbal drugs are currently sold in health food stores with a turnover of about 4.4 billion in 1996, which is anticipated to double by the turn of the century. In India, the herbal drug market is about $1 billion and the export of plant-based crude drugs is around $80 million\textsuperscript{7}. Herbal medicines also find market as nutraceuticals whose current market estimated at about $80-250 billion in USA and also in Europe\textsuperscript{8}.

Germany is the leading country in Europe followed by France in the use of botanicals. Around 80\% of German physicians prescribe herbs and \textit{St.John’s Wort} is a commonly prescribed in mild to moderate depression. Similarly, \textit{Ginkgo} is a hot selling botanical in Europe. The cost of about 40\% of the herbal remedies prescribed by German physicians is covered by the healthcare system\textsuperscript{9}. In USA, a large Center of Complimentary and Alternate medicine has been established recently at the NIH (National Institute of Health), with heavy funding and more recently, NIH has been engaged in sponsoring studies on large clinical trials on botanicals such as \textit{St. John’s Wort} and \textit{Ginkgo}\textsuperscript{10}.

Medicinal plants play a vital role for the development of new drugs. During 1950-1970 approximately 100 plants based new drugs were introduced in the USA drug market including deseridine, reseinnamine, reserpine, vinblastine and vincristine which are from
higher plants. From 1971 to 1990 new drugs such as etoposide, E-guggulsterone, Z-guggulsterone, teniposide, nabilone, plaunotol, lectinam, artmisinin and ginkgolides appeared all over the world. 2% of drugs were introduced from 1991 to 1995 including paclitaxel, toptecan, gomishin, irinotecan etc. Plant based drugs provide outstanding contribution to modern therapeutics; for example: serpentine isolated from the root of Indian plant *Rauwolfia serpentine* in 1953, was a revolutionary event in the treatment of hypertension and lowering of blood pressure. Vinblastine isolated from the *Catharanthus roseus* is used for the treatment of Hodgkins, choriocarinoma, non-Hodgkins lymphomas, leukemia in children, testicular and neck cancer\textsuperscript{11,12}. Phodophyllotoxin is a constituent of *Phodophyllum emodi* currently used against testicular, small cell lung cancer and lymphomas. Indian indigenous tree of *Nothapodytes nimmoniana* (*Mappia foetida*) are mostly used in Japan for the treatment of cervical cancer.

Most currently marketed natural product-based drugs were identified before the introduction of high-throughput screening and bio- and chemo-informatics. Since, the introduction of high-throughput screening in many companies, natural products have become gradually, but inexorable, deprioritised in favour of combinatorial synthetic libraries. This fact may explain, at least in part, the dearth of high quality lead compounds generally recognized throughout the industry. The number of potential new drug targets emerging from the Human Genome Project and microbial genomics is now set to increase dramatically and the high-throughput screening technologies are already in place to accommodate them. Molecular diversity thus becomes the rate limiting factor in determining how productive these new screens will be driven by these considerations the prospects for natural products to deliver drug leads are probably greater than in the recent
past. Increasingly available as pure compounds, natural products are highly amenable to the much broader screening opportunities presented by the plethora of the targets. While the rapid identification of a lead compound or lead compound series remains the primary objective of all high-throughput screening regardless of chemical library input, natural products are uniquely well placed to provide structural information from which virtual compounds can be created by computational chemistry and allied technologies\textsuperscript{13}.

Part of the future direction for natural products, therefore, also lies in using structural chemical databases in conjunction with those of target proteins and genes and contributing to the generation of new chemical entities through computational molecular modelling. With their structural versatility, natural products can be expected to play a major role in the ongoing transition from empirical drug screening to rational drug designing.

India is one of the 12 mega biodiversity centres having over 45,000 plant species. Its diversity is unmatched due to the presence of 16 different agro climatic zones, 10 vegetative zones and 15 biotic provinces. The country has 15,000-18,000 flowering plant, 23,000 fungi, 2500 algae, 1600 lichens, 1800 bryophytes and 30 million micro-organisms. India also has equivalent to three fourth of its land exclusive economic zone in the ocean harbouring a large variety of flora and fauna, many of them with therapeutic properties. About 1500 plants with medicinal uses are mentioned in ancient texts and around 800 plants have been uses in traditional medicine. However, most of these plants have not been screened systematically to prove their ethnomedical uses, to isolate the active ingredients and to develop them as drugs or lead molecules for drug development.
Health can be defined as homeostatic condition of physical, mental and social behaviour. Any change in the physiology of an individual without the involvement of infecting organism is known as a disorder and with involvement of infecting organism is known as a disease. Hence the occurrence of a disorder / disease is an old as the origin of human beings and requires remedial measures in the form of medical treatment given in various system like naturopathy, homeopathy, ayurveda, unani and allopathy etc. from the earliest times, herbs have been prized for their pain relieving and healing abilities and today we still rely on the curative properties of plants in most of our medical system. Some of these tradition and medical practices may seem strange and magical, others appear rational and sensible, but all of them are attempts to overcome illness and enhance the quality of life.

The disease, decay and death have always been coexisted with life and hence the study of diseases and their treatment must also have been contemporary with the dawn of human intellect. The primitive man must have used as therapeutic agents and remedial measures those things, which he was able to procure most easily. There is no authentic record of drugs used by primitive man. The Vedas are the earliest sacred books of India of which there are four; rigveda, yajurveda, samaveda and atharvaveda. Although there is no definite evidence that suggests its exact period of origin the vedic period in Indian history goes back to over 5000 years. The history of medicine in India can be traced to the remote past. The earliest mention of the medicinal use of plants was found in rigveda, perhaps the oldest repository of the human knowledge.

Ayurveda is the term used for the traditional medicine of ancient India. “Ayur” meaning life and “veda” meaning study. The ayurvedic classics include Charak samhita,
dealing with internal medicine and susruta samhita, dealing with surgery\textsuperscript{14}. In ayurveda herbal preparation and oxides of metals are usually used as drugs. Even today ayurveda dominates the modern system of medicine particularly for the treatment of chronic diseases in India\textsuperscript{15}.

In practice ayurveda is a dynamic phenomenon that offers multifaceted approach to healing and emerge as a plural medicine system in itself\textsuperscript{16}. It is estimated that, 7500 plants are used in local health traditions (ayurveda and naturopathy) mostly in rural and tribal villages of India. Out of these, the real medicinal value of over 4000 plants is either little or unknown to the main stream of population\textsuperscript{14}. Thus ayurvedic database allows a drug researcher to start from clinically well tested and safe biological material.

Recent well documented reviews highlight the importance of herbal drugs. It is also clear from the chronic modern medical treatment and the difficulty / failure to treat diseases such as cancer, cardiovascular diseases, diabetes, rheumatism and newer diseases like AIDS demand new effect drugs\textsuperscript{17,18}.

Moreover, problems with drug resistant microorganisms, side effects of modern drugs and emerging new diseases for which no effective drugs are available, have encouraged their new interests once again to re-examine plant remedies described in the ancient and medicinal tests as a significant source of new drugs\textsuperscript{19}. To mention a few, quinghaosu, artemisenin are from diverse tradition and neem and turmeric are from ayurvedic system. A detailed pharmacological investigation of these plants used traditionally can lead to the development of invaluable plant drugs for many dreaded diseases of digestive, respiratory, renal cardiovascular and endocrine systems. Although
herbal drugs continued to be produced in every country, the clinical efficacy of them was usually not evaluated on scientific basis and the composition of these complex mixtures was only crudely analysed.

Herbal medicines are popular remedies for diseases and play a key role in the human healthcare of a vast majority of the world’s population. According to WHO as much as 4 billion people / 80% of the world’s population rely on the use of traditional medicine, which is predominantly based on plant material (WHO, 1993). Although herbal medicines are effective in the treatment of various ailments, very often these drugs unscientifically exploited and / or improperly used. Therefore, these plat drugs deserve detailed studies in the light of modern science. The WHO also has recognised its importance and has been actively preparing the guidelines and setting the standards in the manufacture of herbal medicines.

The importance of herbal medicine once again is increasing day by day even in western countries and some are still available as prescription drugs in Europe. According to survey by Gosselin during 1962, over forty percent of all the new prescriptions contained a drug originated from natural sources as the ingredient or as one or two more important ingredients. It is interesting to note that the Americans paid estimated $ 21.2 billion for services provided to alternative medicinal practitioners.

Herbal formulations, which have reached widespread acceptability as therapeutic agents in India, include antidiabetics, nootropics, hepatoprotective and lipid lowering agents. Two streams of natural systems of medicine in India have been percolated through centuries till today. The first stream of natural medicine is based on an empirical
experience with various kinds of herbs as regards to their healing abilities. Such usage has no logic on the nature of a specific biological activity. Such approach of medicine is termed as Ethnomedicine, as such healthcare practices are mostly limited to specific ethnic communities the often stream of natural medicine is scientific with an objective to expand the therapeutic resources within the nature, it tries to understand the logic that governs the chemical or biological activity of various agents. Its approaches are aimed at the propagation of a scientific evaluation of empirical experience rather than spreading a mere belief on a particular remedy. This stream of medicine is termed as ayurveda which was mentioned earlier.

The concept of ethnopharmacology evolved from the requirement for studies in the light of modern sciences on the drugs used in the traditional medicines. It is defined as the inter disciplinary science of biologically active agents traditionally observed by man. India has a vast ethnobotanical knowledge since ancient times. Origin of all such knowledge in India is from the great tradition of ayurveda, which is a living tradition of medical practice even today. Many plant derive drugs used in modern medicine are developed by ethnobotanical approach leads to subsequent ethnopharmacological studies. Scientific studies available on a good number of medicinal plants indicate that promising bioactive constituents can be developed for many problems of health. The pioneering research on indigenous medicinal plants in India was initiated by Sir Ramnath Chopra and was well documented in his comprehensive treatise. Later multidisciplinary research on indigenous medicinal plants was done by the Indian council for ayurveda ad siddha in the Council for Scientific and Industrial Research (CSIR) laboratories. A good number of medicinal plants have been
investigated and are well documented \textsuperscript{27,28}. However most species of higher plants have been described, nor surveyed for chemical or biological activities of their constituents. All the plant derived drugs (nearly 119) used worldwide came from fewer than 90 of the 2,50,000 plant species that have been identified\textsuperscript{16}.

In future, plant derived chemicals that are biologically active can be suspected to play an increasingly significant role in the commercial development of new drugs. The study of medicinal plants and development of drugs from these natural sources has not received much attention it deserved. The problem with herbs therapy are,

- The required herb does not exist universally because of geographically varied environmental conditions
- It may not grow in all seasons leading to lack of availability in some seasons
- There may be qualitative variations in active constituents because of seasonal variation even at the same source
- There may be genetic variation in the same place or from plant to place
- Storage in raw forms creates more problems
- A single herb may not be adequate to produce required response
- It is difficult to assess the correct therapeutic dose
- Inadequate scientific approach etc

Hence, it is advisable to prepare the cataracts, identify the chemical constituents and standardise them by biological means and evaluate for its biological response and optimise the dose for the required therapeutic response in preclinical / clinical studies.
Need for the study:

Natural products have been playing a vital role in health care for decades. Of the different sources of natural products, plants have been a source of chemical substance, which serves as drugs in their own right or key ingredients in formulation containing synthetic drugs. The process that leads from the plant to pharmacologically active, pure constituent is every long and tedious and requires a multidisciplinary approach. The selection of the plant species is a crucial factor for the ultimate success of investigation. Through random selection gives some hint, targeted collection based on chemotaxonomic relationships and ethnomedical information derived from Tradition Medicine are more likely to yield pharmacologically active compounds.

Though the advances in modern medicines are significant, there remains an ever increasing demand for herbal medicines. Effective and potent herbal medicines require evaluation by standard scientific methods so as to be validated for the treatment of diseases. The presents of patent laws have increased the necessity to preserve the claims of these time-tested folk medicines. Thus, it has become imperative to initiate steps to document components and activity of these medicinal plants.

The pancreas is comprised of separate functional units that regulate two major physiological functions these are digestion and glucose metabolism. The effects of diabetes mellitus include long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, heart, and blood vessels. Diabetes may present with characteristic symptoms such as thirst, polyuria, blurring of vision, weight loss, and polyphagia, and in its most severe forms, with ketoacidosis or nonketotic hyperosmolarity, which, in the absence of effective treatment, leads to stupor, coma, and
death. Often symptoms are not severe or may even be absent. The number of adults with diabetes in the world are estimated to rise from 135 million in 1995 to 300 million in 2025. An estimated 150 million people have T2DM globally. This figure is expected to double by 2025. The WHO estimates that 75 percent of the 300 million adults with diabetes in 2025 will live in developing countries. It’s projected that the number of people with diabetes in developed countries will rise 42%, from 51 million in 1995 to 72 million in 2025. The number of people in developing countries with diabetes will increase by more than 2.5 times (170 %), from 84 million in 1995 to 228 million in 2025.

Hence, in the present study, we were interested in carrying out a systemic phytochemical, biological, pharmacological evaluation of Mollugo oppositifolia, Smilax perfolita and Flemingia wightiana which were used traditionally for the treatment of anti diabetes.
BIBLIOGRAPHY


