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A Brief Review on Medicinal Plants from South India, Endophytes and their Antidiabetic Properties

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ABSTRACT

This paper seeks to review the potential treatment of diabetes with a focus on novel therapeutic effects produced by endophytic fungi that are associated with certain plants. Diabetes is a growing concern among the Indian population, and as a result, there has been an increasing amount of research done to discover new drugs and remedies. South India, with its unique geographical terrain is conducive for the growth of several indigenous plants that have medicinal properties. These plants are known to also be associated with some fungal strains that have metabolites with potentially anti-diabetic properties. This review looks at such plants, and how best to grow endophytic fungi accordingly.

Key Words: Diabetes mellitus, Endophytic fungi, Medicinal plants, South India

INTRODUCTION

There is currently a growing need for compounds of high potency and low toxicity with therapeutic properties for various medicinal applications. This, along with the search for microbial drug resistance has led to great interest in the research of endophytic fungi. Endophytes collectively refer to those fungi and certain bacterial strains exhibiting a mutualistic relationship with a host organism, thereby preventing the entry of a variety of pathogens into the host. As a result of years of co-evolution coupled with some degree of genetic recombination, endophytic fungi possess biosynthetic capabilities greater than that of the host organism.(1) This manifests as them being a source of novel organic compounds with unique biological activities- including anitbiotics, antimycotics, immunosuppresants, anticancer and antidiabetic ones.

Endophytes

Endophytes describe those microorganisms which inhabit healthy tissues of living plants, but do not result in any apparent symptoms of diseases. They are found loaded in some part or the other of every plant. Studies have shown that there exists a balance between the host's defence mechanism and the virulent nature of the endophyte. Although they usually do not cause any disease, if there is any disturbance in this balance, a disease condition can develop.(2) Endophytes often produce various metabolites, and the properties of these metabolites vary according to the source. Secondary metabolites produced by the endophytes are similar to those produced by the host, as a consequence of genetic exchange.

Diabetes Mellitus: Type II Diabetes

Diabetes mellitus is a group of metabolic disorders that is most commonly associated with one common manifestation in the form of hyperglycaemia- a condition in which there is excessive amounts of glucose circulating in the blood plasma. Chronic hyperglycaemia may damage the eyes, kidneys, nerves, heart and blood vessels.(3) An inherited or acquired deficiency of insulin produced by the pancreas, or the ineffectiveness of the insulin which is produced causes this condition.

The WHO has recently released records of 30 million people who were diagnosed with diabetes in 1985. Since then, the number has increased to more than 171 million in 2000. It is estimated that over 367 million people will suffer from diabetes by the year 2030.(4) Highest incidences of diabetes are predicted to take place in developing countries, between the age groups of 45 and 65.

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Traditional treatment for Diabetes Mellitus

There is a lot of ongoing research to determine methods of chemical treatment and discovering biological drugs in order to treat this condition. Traditionally, metabolites from plants have been used to treat many disorders. India is famous for Ayurveda- a system that stresses the use of plant based herbs and pastes to help cure disorders that are common, helping people maintain a healthy lifestyle.(5)

Technology and an increasing pool of knowledge have led to research being carried out into potential use of drugs from plants.(6) Indian tribes have used various plant species specifically to treat diabetes, as detailed in the literature on traditional phytotherapy of Indian Medicinal Plants. These include- *Asparagus racemosus*, *Butea monosperma*, *Cathanranthus roseus*, *Coccinia indica*, *Gymnema sylvestre*, *Syzygium cumini* and *Momordica charantia.* They are also currently being used in modern medicine.(7)

Endophytes from potential medicinal plants are subject to bioprospecting during isolation as the choice of the plant is important. Metabolites which are produced and screened are usually composed of compounds such as steroids, quinones, coumarins and phenols. Since the early ages, substances that have been harvested from plants have aided towards the treatment of various bacterial and viral infections. With the advent of more research, there is an increasing focus on the endophytes associated the plants as opposed to the plant itself. Medicinal plants are used by 80% of the world to help cure diseases.(8)

Ancient Indian literature such as the Ayurveda has a mention of medicinal plants that possess endophytesto treat various ailments. A few plants that have been specifically reviewed for possessing anti-diabetic activity include *Allium sativum, Allium cepa*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Ficus bengalenesis*, *Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Syzigium cumini*, *Swertia chirayita*, *Tinospora cordifolia* and *Trigonella foenum graecum.(5)* Apart from these, there are about 400 species that have been identified to possess anti- diabetic effects. These plants have antihyperglycemic effects that can help control diabetes mellitus. These effects are due to their ability to alter pancreatic tissue function. This is achieved by either decreasing the absorption of glucose in the intestine or increasing the insulin output or by even facilitating metabolites in processes that heavily depend on insulin.(9)

Novel bioactive compounds extracted from these plants have hypoglycemic effects that are equal to the known oral agents that are used presently. These plants can be further exploited for endophytes and these endophytes can then be tested for production of substances with hypoglycemic activity.(10)

South Indian plants with anti-diabetic properties

Annona squamosa Linn. (Annonaceae), is a plant grown throughout India, and is known as Custard Apple more commonly. The active pharmacological components can be found in the seeds and leaves of the plants. They show both hypoglemic and antidiabetic properties, by increasing the level of insulin from the pancreatic islets. This result in more glucose being utilized in the muscle and output of glucose from the liver being inhibited. Leaves are additionally used to maintain cholesterol levels. Extracts from this plant have a high margin of safety.(11)

Bougainvillea spectabilis Linn. (Nyctaginaceae), is a widely used ornamental plant in India. It traditionally has shown to possess antidiabetic activity, with a potential to lower the blood glucose level. The effect has been reported on streptozotocin-induced type 1 diabetic albino rats.(12) An ethanolic extract of the leaf increases glucose uptake by enhancing the glycogenesis process in the liver as well as the insulin sensitivity. This is an example of antihyperglycemic activity.

Casearia esculenta Roxb. (Flacourtiaceae), is a shrub in South India more widely known as wild cowrie fruit. The root extract of this plant has shown to lower blood sugar levels by influencing metabolism of certain proteins as well as important enzymes. C. esculenta root extract has the hypoglycemic and antihyperglycemic effect. However, it may elevate liver and renal damage.(13)

Cassia kleinii (Caesalpiniaceae), is used by the common folk as a remedy, as well as by some medical practitioners. Phytomedicines have been shown to develop from this plant, as they show antihyperglycemic activity on the glucose feed. It has use in insulin dependent diabetes, while the action that the drug does is similar to that of insulin on glucose metabolism.

Terminalia catappa Linn. (Combretaceae), is the Indian almond plant and is found growing in warmer parts of India. The fruit of this plant with petroleum ether and a methanolic extract has an effect on blood glucose levels. The plant acts via β-cells regeneration. The effect may be due to β-carotine in preventing complications such as glycosylation in diabetic rats.(14)

Table 1: List of notable South Indian plants and their anti-diabetic properties.(7)

Plant Name	Common name/ Herbal Formulation	Anti-Diabetic and other beneficial effects
Annona squamosal	Sugar apple	Ethanolic leaf extract has antihyperglycemic effect

Artemesia pallens	Davana	Reabsorption of glucose is inhibited
Areca catechu	Supari	Utilization of peripheral glucose increases
Beta vulgaris	Chukkandar	Enhances glucose tolerance
Boerhavia diffusa	Punarnava	Antioxidant, plasma insulin level increases, activity of hexokinase increases
Bombax ceiba	Semul	Hypoglycemic
Camellia sinensis	Tea	Antioxidant and antihyperglycemic
Capparis decidua	Pinju	Hypolipidemic, antioxidant and hypoglycemic
Coccinia indica	Bimb or Kanturi	Hypoglycemic and insulin secretogogue
Emblica	Amla	Hypoglycemic and decreases lipid peroxidation
Ficus bengalensis	Bur	Hypoglycemic
Gymnema sylvestre	Gudmar or Merasingi	Antihyperglycemic and hypolipidemic
Hemidesmus indicus	Anantamul	Anti-snake venom activity and anti-inflammatory
Hibiscus rosa-sinesis	Gudhal or Jasson	Triggers insulin release from pancreatic beta cells
Ipomoea batata	Sakkargand	Insulin resistance is decreased
Momordica cymbalaria	Kadavanchi	Hypoglycemic
Murraya koenigii	Curry patta	Enhances glycogenesis and inhibits gluconeogenesis
Musa sapientum	Banana	Antihyperglycemic, antioxidant
Phaseolus vulgaris	White kidney bean	Inhibits alpha amylase activity
Punica granatum	Anar	Antihyerglycemic
Salacia reticulata	Vairi	Alpha glucosidase inhibitor

Optimization of growth of endophytic fungi -

If we wish to investigate the endophytic fungi and their benefits, it is important to cultivate them under the appropriate laboratory conditions. In this regard, isolation is the first step.(15,16) Surface sterilization followed by crushing plant tissues and plating on to a nutrient medium is a commonly used protocol. Sodium hypochlorite, Hydrogen peroxide and ethanol have all been used for this purpose. The plant tissues are usually submersed into sodium hypochlorite and then rinsed with distilled water. If done well, there will be high amounts of growth as there is no damage to the endophytic colonies from sterilization. An efficient surface sterilization results in high amounts of endophytic growth on agar plates which indicates that there is no damage from the sterilization to the endophytic population.

Next, the choice of nutrient medium also could influence the efficiency of the isolation process. For endophytes, there are two types of media used most commonly- one that is complex and rich containing high amounts of undetermined nutrients and another that is minimal, containing much lesser but precise amounts of nutrients. The number of colonies as well as the diversity of endophytes grown is determined by the choice of nutrient media.(17) Studies show that less than 1% of the endophytes are usually cultivable, and some that are grown initially cannot be recultivated later. This is mostly because residual compounds and metabolites specific to certain plants are not present at all stages. Tissues contain some compounds that are not present in the media for growth, but are nonetheless important for their growth.

Both types of media contain elements that are vital for non-selective growth of endophytes. Complex media contains water, carbon sources, salts and a source of amino acids from fungal, plant or animal origin (yeast extract, tryptone, peptone, etc). These are undefined because the composition of the source of the amino acid is unknown. These media are called undefined because the exact composition of the amino acid source is not known.(18) Trypticase Soy Agar (TSA) and Caesin Starch are examples. They have high quantities of nutrients, and hence many dominant strains grow fast and grow over those strains that take longer. Minimal media however provides a precise amount of nutrients leading to selective growth. This mimics the actual conditions of the plant and as a result, might allow the endophytes to adapt easier.(19)

As a gelling agent, Agar is commonly used. However, it might be the case that some fungal strains are unable to grow. To overcome this, gellan gum has been used, as it is a bacterial polysaccharide that is used for human tissue culture. This is produced by *Sphingomonas sp.* Literature reviews have shown a higher amount of endophytic growth on complex media.(20)

DISCUSSION

While there have been several attempts to come up with commercially viable drugs and methods of treatment for diabetes, each of them come with their own set of hurdles and challenges. However, the use of endophytes from natural plant sources as prospective anti-diabetic agents confers various advantages that are otherwise lacking in our conventional approaches to treating the disease. South India's ambi-

ent geographic conditions, both in terms of weather as well as terrain, make it conducive for the growth of innumerable varieties of plants, and as a result- an even larger number of endophytes associated with them. It is imperative that our research focus shifts to the use of these plant sources, as it may be possible to scale up their pharmaceutical activity as anti-diabetic agents into sustainable drugs by optimizing the conditions for their growth, cultivation and isolation.

CONCLUSION

A lot of medicinal plants have been under research for treatment of various disorders, be it common flu, HIV or diabetes. But due to the risk of increasing microbial resistance to the already existing drugs, there has been shift from plant metabolites to endophytic metabolites for treatment of different kinds of disorders. The easy availability of endophytes throughout the plant is a major advantage. Extraction and isolation of specific endophytes thus becomes a relatively simple process. Another important thing to note is the relation between the source of the endophyte and endophyte itself. The plants that are known to have specific pharmaceutical importance will definitely possess endophytes with similar properties. Therefore, the main area of focus is the endophytes collected from medicinal plants known to possess anti-diabetic properties. South India is a rich source of medicinal plants and there have been various literatures and manuscripts that talk about the same.

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Abbreviations Used

WHO: World Health Organization.

HIV: Human Immunodeficiency Virus.

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