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AN ARTICLE ON DIABETIC WOUND HEALING ACTIVITY OF VARIOUS HERBAL PLANTS

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Abstract:

Diabetes is a disease that occurs when blood sugar level is too high. It is caused by insufficiency of insulin hormone that is secreted from pancreatic β cells. A wound is a break or damage in any body tissue where violence is understood by any action of external agency. In case of diabetes, wound can take longer time to heal that can increase risk of infections and other complications. People who experience poor wound healing due to the effects of diabetes on the nerves and blood vessels might also experience other complications. Some complications include heart disease, kidney disease, and eye problems. They can also have developed foot ulcers, diabetic foot ulcers are a non-healing, chronic complication of diabetes that may lead to high hospital costs and in extreme cases leads to amputation. Diabetic neuropathy, abnormal cellular activity, peripheral vascular disease are also the main factors that have effects on diabetic wound repairing. Many herbal plants are used in the healing of diabetic wound and related complications. These are always good and safe for use. Herbal drugs do not have any side effects.

Keywords: Diabetes, Epidemiology, Etiology, Wound healing, Herbal plant.

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1. INTRODUCTION:

1.1 Diabetes :

Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretary response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemas [1]

Diabetes mellitus (DM) is commonly referred to as a “sugar” and it is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance) [2]

The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025

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Diabetes is a chronic disease that occurs either when the β cells of pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that keeps blood sugar maintained. Diabetes mellitus is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity. It estimated that the total number of diabetic patients can be around 40.9 million in all over India and this can be 69.9 million by the year 2025.^[1]

There are some different types of diabetes:

Insulin Dependent Diabetes Mellitus (Type1 IDDM)
This type of diabetes mellitus is also called autoimmune diabetes and previously it is known as ketosisprone diabetes or juvenile-onset. The individual may also seek with other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease [5]. Type I diabetes mellitus is also known as insulin- dependent diabetes mellitus (IDDM), this mainly occurs in childrens and young adults; the onset is usually sudden and can be life threatening.

Non-Insulin Dependent Diabetes Mellitus (Type2 NIDDM)

Type 2 diabetes mellitus is also called as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance (American Diabetes Association, 2014). People with this type of diabetes frequently are resistant to the action of insulin. This affects blood vessels, kidneys, eyes and nerves occur in both types and are the major causes of morbidity and death from diabetes.^[6,7]

General symptoms :

- Increased hunger
- Increased thirst
- Weight loss
- Frequent urination
- Blurry vision
- Extreme fatigue
- Sores that don't heal.^[8]

1.1.1 Epidemiology :

The epidemiology of diabetes is understood best in these categories: diabetes in the population, type 1 diabetes, type 2 diabetes, age and diabetes, diabetes and ethnic background, gender and diabetes, and morbidity and mortality associated with diabetes.

Learning Break: Diabetes is typically classified as type 1 & type 2, but there are actually many other

types of diabetes (e.g., gestational, drug-induced, infection-induced, or disease-induced, etc.). However, these represent a very small minority of the total number of cases of diabetes. There is also a condition called pre-diabetes. It is a condition in which the plasma glucose, the HbA1C, and other markers of diabetes are persistently elevated and not high enough to required treatment. Pre-diabetic peoples have an increased risk of developing type 2 diabetes, heart disease, and stroke.

Diabetes in the population: According to a report it estimated that approx. 26 million American peoples have diabetes, and an estimated 79 million American peoples have pre-diabetes (US Department of Health and Human Services, 2011). Diabetes affects 8.3% of American people and 11.3% of people aged 20 years and older and pre-diabetes affects approximately 35% of people with age of 20 years and older than 20.

Type 1 diabetes: Type 1 diabetes reports approx. 5%-10% of all cases of the disease.

Type 2 diabetes: Type 2 diabetes reports approx. 90%-95% of all cases of the disease .

Diabetes and age: Type 1 diabetes typically develops in children aged 4 years and older then 4 years, and the peak incidence in childrens occurs between the ages of 11-13 years. Some cases of type 1 diabetes occurs in adults, and cases of type 1 diabetes have been reported in peoples in the 8th & 9th decade of life. Almost all cases of type 1 diabetes are caused by destruction of the pancreatic β cells, but there are a small number of patients that develop idiopathic type 1 diabetes. This disease is strongly inherited, and the need for insulin tends to wax and wane. It is not caused by an autoimmune process. The incidence of type 2 diabetes increases with age.

Diabetes and gender: Type 1 diabetes is approx. 1.5 times less common in women then men . In US, approximately 11.8% of all men with 20 years age or older have diabetes, and approximately 10.8% of all women 20 years of age or older have diabetes .^{[7][8]}

Diabetes and ethnic background: In ascending order, diabetes affects 7.1% of non-Hispanic whites, 8.4% of Asian-Americans, 11.8% of Hispanics and 12.6% of non-Hispanic blacks. Type 1 diabetes is more common in white peoples ; it is much less common in African-Americans and Asian-Americans. Type 2 diabetes is more common in

Native Americans, African-Americans, and Hispanics than whites.

Diabetes and morbidity and mortality: According to US Department of Health and Human Services, 2011 Diabetes is the seventh leading cause of death in the US. It is the leading cause of neuropathy, non-traumatic amputations , kidney failure, and blindness in adults. In addition, diabetes is considered to be a major risk factor for the development of cardiovascular disease and stroke.^[9]

1.1.2 Etiology:

Type 1 Diabetes

Type 1 diabetes is caused by destruction of the β cells of the pancreas by autoimmune response. This process occurs in genetically susceptible people and is triggered by an environmental factor or factors. When the majority that is approx. 80%-90% of the β cells have been destroyed, the serum glucose increases and signs and symptoms of type 1 diabetes will be seen.

Learning Break: Type 1 diabetes is caused by an interaction of genetics and environment, and there are multiple genetic and environmental factors that may contribute to the development of the disease.

Environmental factors: Environmental factors especially some viruses are play a role in the development of diabetes, and there is some epidemiological evidence that supports this theory. For example, the cases of the disease has been increasing rapidly worldwide, especially in young childrens. However, although there are certainly regional differences in the cases of type 1 diabetes, the genetic risk profile for type 1 diabetes was not different greatly from area to area, suggesting the possibility of an environmental influence on the development of the disease. Environmental triggers that may initiate the destruction of pancreatic β cells by the autoimmune response of body include chemicals, dietary factors in early life “examples : exposure to cows milk, vitamin D deficiency”, cytotoxins, enteroviruses, and many other infections. Aside from the enteroviruses there is some convincing evidence that these environmental factors are responsible for causing the large increase in the number of cases of type 1 diabetes.

Environmental factors/enteroviruses: Enteroviruses are very common viruses. They are spread through infected respiratory particles and stool, and they are second only to rhinoviruses in the number of infections caused. Epidemiological studies have

shown a relationship between the occurrence of enterovirus infections and the development of type 1 diabetes, especially in genetically susceptible individuals. A review and analysis of observational studies exhibit that children with type 1 diabetes were 9 times more having enteroviral infection, and children with autoimmunity that could affect the pancreas were 3 times more having an enteroviral infection.^[9]

Genetic factors: Type 1 diabetes is also a genetic disease. At least 18 regions of the genome have been attached with a risk for having type 1 diabetes. A lot of research has examined the Insulin Dependent Diabetes Mellitus 1 region, a region of the genome that contains the human leukocyte antigen genes, and the greatest genetic risk for type 1 diabetes is related to alleles, genotypes, and haplotypes of genes. The HLA is a region of genes that is located on chromosome 6. These genes encode major histocompatibility complex immune response proteins that are located on cell membranes; these are used by the immune system to detect antigenic material. The genes that encode the MHC proteins that are most strongly related with type 1 diabetes are HLA-DR, HLA-DQ, and HLA-DP, and they have alleles that affect the coding of the proteins that appear as foreign to the immune system. An autoimmune response begins, and the β cells of pancreas are destroyed. Therefore genetics are an important risk component for type 1 diabetes, there are many genes that may be involved and influences the development of type 1 diabetes is still far from clear. For example, in identical twins the risk for one sibling developing type 1 diabetes if the other has the disease is approximately 33%, and children whose parents have type 1 diabetes only have a 3%-6% risk of developing type 1 diabetes.^[7]

Type 2 Diabetes

Type 2 diabetes is specified by insulin resistance and a progressive decline in pancreatic β cell insulin production. There is no autoimmune related pancreatic β cell damage and most patients with type 2 diabetes do not need insulin during the initial stages of the disease. Insulin resistance is a process in which insulin is produced, but is not used in sufficient way: a given amount of insulin does not give the expected response. The decreasing response in pancreatic β cell function is due to decreased β cell mass caused by apoptosis; this may be a result of aging, genetic susceptibility, and insulin resistance itself. The etiology of type 2 diabetes is very complex and includes genetic and lifestyle factors.

Genetic factors: There are susceptibility genes that play an important role in the development of type 2 diabetes, but their contribution shows to be small. The effect of the known, common gene variants in creating a pre-disposition to type 2 diabetes is approximately 5%-10%, so unlike some inherited diseases, being homozygous for these susceptibility genes does not typically result in a case of type 2 diabetes unless certain environmental factors are present.

Lifestyle factors/demographics: Obesity is definitely a major risk factor for the development of type 2 diabetes (Li, Zhao, Luan, et al, 2011), and the greater the degree of obesity, the higher the risk (Nguyen, Nguyen, Lane, Wang, 2011). Excess amount of adipose tissue is in a state of chronic inflammation, and this inflammation is cause insulin resistance in the adipose tissue and in other organs.^[9]

1.2 Wound Healing

A wound is break of the anatomic structure and its useful continuity of residing tissue. Healing is the system of repairing that heal damage of the skin and other soft tissues. Wound healing is a survival process to restore shape and feature. The ability of a wound to heal depends on its intensity of break, as well as on the general fitness and dietary status of the person.

The intense wound is a breakdown of the integrity of the gentle tissue that surrounding any part of the frame. Chronic wound can be understood as wounds that fail to progress orderly and timely sequence of restore.

Wound healing is an intricate process in which the tissue repairs itself after injury. It is a process that involves the activation of inter-cellular pathways, coordination of tissue integrity, and homeostasis. Depending on the nature and depth of the injury, the wound healing can be classified.

1.2.1 Epidemiology

Pressure ulcers are a commonly occurred condition in both acutely hospitalized patients and long-term institutionalized patients. They are estimated to show in approximately 9% of hospitalized patients, usually during the first 2 weeks of hospitalization. This is in state of taking methods to reduce the development of pressure ulcers, that is repositioning, cushioning bony prominence, and using specialized mattresses. In high-risk hospitalized patients, the prevalence of pressure sores is higher, with rates as high as 38%. A study found that even after the use of

a pressure-reducing bed and early nutritional support, 3% of patients in a surgical intensive care unit who were in study developed pressure ulcers. The risk of pressure ulceration in patients annually with neurologic impairment is 5-8%, with a lifetime risk of approx. 85%.

The prevalence of pressure ulcers among patients residing in long-term care facilities has been reported as 2.3-28% and has been an increasingly reason for litigation. Venous ulcers make up 70% of chronic lower end ulcers. The incidence of venous ulcers is approx. 600,000 cases annually in US and the recurrence rate is up to 90%. It estimated that 26.9 million American peoples (8.2% of the population) having diabetes and millions more are increasing. Of those at risk, diabetes is untreated in 8.1 million patients. Diabetic foot lesions are one of the most common causes of hospitalization secondary to a complication of diabetes. Among patients with diabetes, 15% will have a foot ulcer and 12-24% of those with a foot ulcer will require amputation. Indeed, diabetes is the leading cause of non traumatic lower-extremity amputations and accounting for 60% of these amputations in US.^[10]

1.2.2 Etiology

Normally, factors that commonly affect wound healing can be memorized by using the mnemonic device DIDNT HEAL, as follows:

- D = Diabetes: The long-term effects of diabetes lower the wound healing by decreasing arterial inflow.
- I = Infection: Infection potentiates collagen lysis. Bacterial contamination is a compulsory condition but this is not enough for wound infection. A strong host and wound environment are also required.
- D = Drugs: Steroids and anti-metabolites delays the proliferation of fibro blasts and collagen synthesis.
- N = Nutritional problems: Deficiencies of proteins, vitamins A, C, and zinc impair normal wound-healing mechanisms.

- T = Tissue necrosis, resulting from radiation injury and systemic ischemia or local ischemia, delays wound healing. Tissue generation is more important for wound healing.
- H = Hypoxia: Insufficient tissue oxygenation due to local vasoconstriction resulting from sympathetic over reactivity may occur because of blood volume deficit, unrelieved pain, or hypothermia, especially involving the distal extent of the extremities.
- E = Excessive tension on wound edges: This leads to low tissue regeneration.
- A = Another wound: If there are many numbers of wound, there will be competition for the substrates required for wound healing, that decreases the rate of wound healing at all sites.
- L = Low temperature: The relatively low tissue temperature in the parts of the upper and lower extremities is responsible for poor healing of wounds at these sites.^[10]

1.3 Diabetic Wound Healing

If a person has diabetes, then wounds can take longer time to heal. This can increase the risk of infections on wound and develop other complications.

Blood sugar level of body is the main factor in the quick healing of wound. When blood sugar level of body is higher than normal, it can :

- prevents oxygen and nutrients to energizing cells
- prevents immune system of body from functioning efficiently
- increases inflammation in the cells of body
- These all effects slow down healing of wounds.

Many diabetic peoples have problems with immune system activation. The immune fighter cells are activated to heal wounds, but during diabetes their ability to take action, is often reduced. If immune system of body can't work properly, the wound healing will get slower and the risk of infection will high.

1.4 Some plants with diabetic wound healing activity

Common name	Botanical Name & Family	Chemical Constituents	Uses	Mechanism of Action	Ref .
Gulmehendi	Name - <i>Rosmarinus officinalis</i> Family - Lamiaceae	➤ Rosmarinic acid ➤ camphor ➤ caffeic acid ➤ ursolic acid ➤ betulinic acid ➤ carnosic acid	➤ Relieve pain ➤ As antioxidant ➤ As Anti-inflammatory ➤ As antimicrobial agent	This rosmarinic acid was incorporated into meat reporting antibacterial activity against Brocho thrixthermosphacta and Enterobacteriaceae.	[7]
Sadabahar	Name - <i>Catharanthus roseus</i> Family - Apocynaceae	➤ vincristine and vinblastine ➤ ajmalicine ➤ Lochnerine catharanthine ➤ vindoline	➤ to treat lymphomas ➤ to treat Hodgkin's disease ➤ treat non-Hodgkin's lymphomas ➤ to treat Acute lymphocytic leukemia	The vinca alkaloids inhibit cell division by blocking mitosis; they also inhibit purine and RNA synthesis causing death of rapidly dividing cells.	[11]
Gotu Kola	Name - <i>Centellaasiatica</i> Family: Apiaceae	➤ Pentacyclic triterpenoids ➤ brahmoside ➤ asiatic acid ➤ brahmic acid ➤ centellose ➤ madecassoside	➤ leprosy ➤ lupus ➤ varicose ulcers ➤ eczema ➤ psoriasis ➤ diarrhoea ➤ fever	Gotu kola increase collagen production, which is important for wound healing.	[12]
Gwarpatha	Name - <i>Aloe barbadensis miller</i> Family: Asphodelaceae	➤ glycosides ➤ proteins, ➤ lipids, ➤ amino acids, ➤ vitamins, ➤ enzymes, ➤ inorganic compounds	➤ Heals burns ➤ Improves digestive health ➤ Promotes oral health ➤ Clears acne ➤ Relieves anal fissures ➤ Liver function ➤ For constipation ➤ For clear skin.	Glucomannan, mannose-rich polysaccharide, and gibberellin hormone, interconnect with growth factor receptors on the fibroblast, which will increase collagen synthesis after topical application.	[13]
Chinese foxglove	Name - <i>Radix Rehmannieae</i> Family: Orobanchaceae	➤ vitamins A, B, C, and D, ➤ catalpol, ➤ iridoid glycoside	➤ chronic glomerulonephritis	Rehmannia is effective in promoting wound healing through the process of tissue generation, angiogenesis and inflammation control.	[14]

Anaar	Name - Punicagranatum Family - Punicaceae	<ul style="list-style-type: none"> ➤ punicalagins ➤ delphinidin ➤ pelargonidin glycosides ➤ prodelphinidins ➤ seed oil contains ➤ punicic acid ➤ oleic acid 	<ul style="list-style-type: none"> ➤ Antioxidants ➤ Cancer prevention ➤ Alzheimer's disease protection ➤ Anti-inflammatory ➤ Heart disease ➤ Antiviral ➤ Diabetes 	Produce high density of collagen with a good arrangement, which is accompanied by a complete and mature epithelium, low number of inflammatory cells, and angiogenesis.	[15]
Ramfal	Name - Annona squamosa Family - Annonaceae	<ul style="list-style-type: none"> ➤ diterpenoid alkaloid atisine ➤ alkaloids oxophobebine ➤ reticuline ➤ methylcorydaldidine 	<ul style="list-style-type: none"> ➤ dysentery and urinary tract infection ➤ applied to wounds ➤ Prevents Asthma ➤ Regulates Sugar Level 	A. squamosa L. increased cellular proliferation and collagen synthesis by increase in DNA, protein and total collagen at the wound site.	[16]
Indian coral tree	Name - Martynia annua Family - Martyniaceae	<ul style="list-style-type: none"> ➤ glycosides ➤ flavonoids ➤ anthocyanins. ➤ cyanidin-3-galactoside ➤ snapic acid ➤ gentisic acid 	<ul style="list-style-type: none"> ➤ In epilepsy ➤ dysentery ➤ worm infestation ➤ constipation ➤ haemorrhage ➤ antibacterial infection 	Martynia annua shows wound healing by collagen synthesis.	[17]
Pitaya	Name - Selenicereusundatus Family - Cactaceae	<ul style="list-style-type: none"> ➤ β-amyrin ➤ γ-sitosterol ➤ octadecane ➤ Heptacosane ➤ campesterol ➤ nonacosane ➤ trichloroacetic acid 	<ul style="list-style-type: none"> ➤ Cancer. ➤ Heart disease. ➤ High blood pressure. ➤ High cholesterol. ➤ Obesity. ➤ Wound healing. 	It produces increases in hydroxyproline, tensile strength, total proteins, DNA collagen content and better epithelialization thereby increasing healing.	[18]
Papeeta	Name - Carica papaya Family - Caricaceae	<ul style="list-style-type: none"> ➤ papaya pulp contains 88% water, ➤ 11% carbohydrates, ➤ negligible fat ➤ protein ➤ vitamin C ➤ folate 	<ul style="list-style-type: none"> ➤ preventing and treating gastrointestinal tract disorders, intestinal parasite infections, diuretic 	Enzymes that is papain and chymopapain present in papaya do removal of necrotic debris and facilitate development of healthy granulation tissue.	[19]

CONCLUSION:

India is enriched with wide variety of herbal plants with medicinal activity and these can be converted in pharmaceutical preparation that can be used in various diseases. Wound healing activity of various herbal plants during diabetes have recorded some valuable effects as well as they minimize risk of infections on wounds. Diabetes is a chronic disease

which in the result of insufficient amount of pancreatic β cells. This cause difficulties in healing of wounds. Slower healing of wound during diabetes is the worst problem of people now a day. In this review find the various herbal plants which are used in diabetic wound healing. These drugs contains some active constituents which helps to heal the diabetic wounds.

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