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Herbal Nanotechnology: An Effectual Oxidative Stress Reduction Initiative for Hyperglycemic Complications

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Abstract

Diabetes and its impediment has been the major cause for various issues ranging from getting the cells self-targeted in vital organs to the routine quality of life. The complications in diabetes has been on focus in recent times, since it turns to be more violent and end up with more serious degenerative metabolic disorders. The cause of concern for the permanent damaging of the vascular tissues and its network, has been observed mainly due to ROS (reactive oxygen species) or Oxidative Stress. As for as the Diabetic treatment is concern, the effective generation of insulin to suffice glucose procuction and combating the ROS generation would provide awesome advantage. So the aforementioned approach would go hand in hand. Conditions, augumenting the diabetes with ROS production tends to detoriation of the cell function, atherosclerosis, delayed wound healing etc. Long since the evidence of using herbal drugs and its delivery methods are in extinction. As the antioxidants presence in plants in the form of flavonoids, polyphenols and so on, would be an alternative approach to scavange and safeguard the cells from free radicals produced in the body. In this platform the complications of dibetes in relation to oxidative stress and herbal nanotechnology to treat such problems are discussed.

Keywords : *Diabetic complications, Reactive oxygen species, antioxidants, herbal nanotechnology*

Introduction

Basically diabetes is characterized by hyperglycemia, a condition of lack of insulin and development of complications in nephrons of kidney, peripheral nerves and retinal damages. Considerable effect on heart has also be the problem of developing further complications leading to atherosclerotic threats to brain, myocardium and lower extremities [1]. Hyperglycemia causes various kind of injury to vascular system viz, increased pace of high glucose flux, intracellular production of advanced glycation products, activation of protein kinase and abnormal hexoseamine pathway. The increased mitochondrial reactive oxygen species (ROS) would lead to microvascular changes heart and other vital functions of organs and their complex pathways [2, 3]. The damage breaks out by ROS production both mitochondrial and non-mitochondrial results in, tumor formation, age-related degeneration, inflammatory conditions and diabetes mellitus [4, 5, 6]. Better understanding of ROS production and its intervention strategies leading to solution to this problem with newer technologies. In this context major factor for onset of diabetes has been evidenced due to ROS generation [7]. Further various animal studies confirm that embryos are more vulnerable to the oxidative stress especially in type 2 diabetes. Maternal abnormalities were developed and observed to be more prominent in heart and reduction in pregnancy of the animals has been notified [8]. The existing methods of treating diabetes do not combat diabetic complications, so there is an increased need for effective treatment, which is essential to fight with diabetic complications in relation to considerable reduction of ROS by using various technology and herbal drugs.

Consequences for Insulin Resistance and ROS production

In a condition pertaining to the high plasma levels of glucose and free fatty acids leads to increased production of reactive oxygen species (ROS) and to a least of reactive nitrogen species (RNS). In turn the initiation of various kinases starts occurring; proceed to phosphorylation of the insulin receptor and nitric oxide generation [9, 10, 11]. Both the aforementioned pathways cause the signaling of insulin and suppress it drastically. Cascading reactions lends increased insulin resistance in liver, skeletal muscle and adipose tissues [12].As shown in the Fig 1. Increased free fatty acid level and lipid content are the prime factor for insulin resistant type 2 diabetes. Besides, the production of ROS could be more due to free fatty acids are common and mitochondrially how ROS is produced is still not understood and yet to be explored.

ROS and associated Hypertension

The considerate onset of hypertension is due to the non-phagocytic NAD(P)H oxidase (Nox1, Nox 2 and Nox 4), apart from other factors for increased diabetic and hypertensive complications such as mitochondrial generation, inflammation, hypertrophy apoptosis, fibrosis, angiogenesis and rarefaction. Miscellaneous occurrence for ROS bounds to xanthine oxidase, cyclooxygenase, lipoxygenase and nitric oxide synthase. As shown in the Fig 2. Normal physiological processes affected by ROS are immunity, endocrine functions, embryogenesis and signal transduction at cellular level [13]. The intervention has given a tool to effectively control the ROS generation by antioxidants or nitric oxide production, to minimize the vascular injury, renal dysfunction and prevent target organ damage in diabetes and hypertension

Delayed Wound Healing Pattern – Increased ROS

Scoring up of ROS generation would lead to delayed wound healing, as it is the significant clinical problem to deal with to treat with different approach. Antioxidants have forecasted evidence for healing process to be very effective if it is provided. a study has provided robust substantiation in cultured fibroblast, a diabetic phenotype and IGF1, which promotes wound healing on exposure to antioxidants. Pre-treatment of antioxidants increased the IGF1 has brought down diabetic complication and accelerate wound healing [14].

Basis for Diabetic and ROS

Long term diabetic causes are

i. Excess nourishment (Food)
ii. sedentary life style
iii. genetic or miscellaneous factors

All the above conditions leads to glucose and fatty acid overload, in addition the reaction of glucose with plasma proteins forms glycation end products and ROS. The ROS which in turn causes increased non-availability of nitric oxide, increased inflammatory mediators and modification of lipoproteins in atherosclerotic condition [15].

Common complications of diabetes due to ROS are

i. development of insulin resistance
ii. β- cell dysfunction
iii. type 2 diabetes
iv. increased glucose tolerance

Diabetic Nephropathy and ROS

ROS play an important role in commencement and progression of diabetic nephropathy. The roles of oxidative stress in pathogenesis of diabetes complications are evidenced. Vulnerability to glomeruli and retina is observed in patients with insulin resistance diabetes. A ROS-regulated signaling pathway leads to extracellular matrix (ECM) deposition in diabetic kidney was evidenced. ROS are increased in the glomeruli isolated from streptozotocin diabetic rats, providing a direct evidence of increased ROS in diabetic glomeruli.

An approach positively controls the nephritic damages are the treatment with antioxidants. As Antioxidants effectively inhibit high glucose and H_2O_2 induced activation in case of diabetic nephropathy, which would favor patients [16]. The effect of antioxidant therapy is well documented in cell and animal studies, although convincing evidence for clinical efficacy is still lacking.

Exhaustive glycemic control and inhibition of angiotensin II delay the onset and progression of diabetic nephropathy, in part, through prevention of overproduction of ROS [17]. Antioxidants have been shown to prevent or delay the onset of diabetic nephropathy and its progression.

Role of ROS in insulin resistant type 2 diabetes

Receptor level binding of insulin at cell surface leads to the phosphorylation and various signaling pathways, which has been affected by ROS with increased insulin resistance and pancreatic cell dysfunction [18,19]. Therapy with antioxidants like N-acetyl-L-cystine and taurine prevents the hyperglycemia induced by insulin resistance. In patients with type 2 diabetes, acute and chronic administration of lipoic acid, antioxidant, improved insulin resistance [20].

Role of Herbal antioxidants in ROS

The damaging effects of ROS is tackled effectively by antioxidants, normally superoxide and hydrogen peroxide are produced in the body. If excess quantities of generation leads to pathological ROS production. Many herbs has the potential to compromise ROS such as green tea, grape seed, ginseng and Scutellaria baicalensis. Long while herbal medicines used for the diabetes has been in existence. Current pre-clinical and clinical studies have demonstrated that many of them exhibit potent anti- inflammatory and anti-oxidative properties, and have also identified the active phytochemicals responsible for their activities. The herbal medicines and nutraceuticals, as well as their bioactive components, which exhibit anti-inflammatory and anti-oxidative properties, provide a promising approach for the prevention and treatment of diabetic complications [21]. The etiology of diabetes and its complications are because of free radicals and for the reason herbs with antioxidant properties are believed to possess faith in controlling and minimizing the damage due the reactions. The list of some herbs used for diabetes and its complications are given in Table 1[22]. Nearly 400 herbs are accounting for diabetes treatment worldwide.

Acacia arabica (Babhul) has got anti-diabetic agent shown to have hypoglycemic effect. Aegle marmelos (Bengal Quince) which improves digestion and reduces blood glucose, urea and serum cholesterol level. Allium cepa (Onion) is a potential antioxidant, anti hyperglycemic and anti hyperlipedemic activity. Allium sativum (Garlic) has been used to increases insulin secretion and controls lipid peroxidation. Aloe vera stimulates β cell to secrete insulin, Anti-inflammatory and wound healing [23, 24, 25]. Azadirachta indica (Neem) evidenced using anti-hyperglycemic, hepatoprotective and antioxidant activities. Eugenia jambolana (Jamun) is a viable anti-hyperglycemic agent. Mangifera indica (Mango) is a anti-diabetic agent, reduces intestinal glucose uptake. Momordica charantia (Bitter gourd) is utilized as antidiabetic and antihyperglycemic Agent. Ocimum Sanctum (Holy basil) cause glucose level decline in fasting condition, triglyceride and total lipid content. Phyllanthus amarus (Bhuiawala) is a antinflammatory, anticancer, antioxidant and antidiarrhoeal. Certain formulations available for the diabetic treatments are given table 2

Bao H et al studied icariin a flavonoid of Epimedium pubescens known to have considerable antioxidant activity [26]. They demonstrated cardiac functions and mitochondrial oxidative stress in streptomycin induced diabetic rats. The observations are in favor of controlling oxidative stress of cardiac complications in diabetes induced animal. An 8 weeks of administration markedly improved cardiac function and ROS has been proved effectively [27].

Nanotechnology

The nanotechnology is facing expansions in all dimensions for serving mankind, that almost all the countries are striving to explore for the social well being and economy of the country. Nanoparticles are known to have tremendous applications in the field of diagnosis and theraphy. Such imperative nanoparticles have very great trait to carry and serve like an antioxidant, antihyperglycemic and ROS interfering action [28]. Treatment of antidiabetic potent nanoparticle with plants would have therapeutic value do create a new platform for herbal medicines in nanoscience for drug delivery [29]. Intentions of few antidiabetic nanoparticles of herbal origin are discussed. the options for herbal nanotechnology is shown in the fig 3.

Nanoparticles of antioxidant potential Cuscuta chinensis

Feng lin et al have demonstrated the preparation of nanosuspension of Cuscuta chinensis, since its principles are majorly flavonoids which has got poor solubility. It drives them to make it more soluble formulation. The prepared formulations are tested with acetaminophen induced hepatotoxic rats. As the flavonoids are known to have antioxidant which has the caliber to control oxidative stress these components (flavonoids) are taken into account in this study. They observed

only 50mg/kg of body weight of nanosuspension containing Cuscuta chinensis, effective than 125mg/kg weight administered from ethanolic extract of same drug. In this context suggestions are given to increase the tough molecules solubility enhancement through nanotechnology [30]

High antioxidant activity of Dalbergia sissoo (Indian Rosewood)

Nayan Roy et al studied extracts of the plant stem bark, they intervened to extend they work towards invitro antioxidant determination by chemical method, using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity. In their experimentation of aqueous and methanolic extract they found aqueous extact has greater activity. They concluded that plant has high antioxidant activity and it may find it very useful in the treatment of diseases and complications caused by oxidative stress [31].

Nanoencapsulation of Albizia chinensis

Avnesh kumar et al explained the nanoencapsulation of the herb having potential antioxidant activity of its content quercitrin. The polymer poly-D,L-lactide (PLA) is used to encapsulate the material and solvent evaporation technique was deployed to prepare the nanodimensions of the drug. The drug quercitin was made to encapsulate to increase the solubility, permeability and stability of the molecule. Moreover, the properties of nanomedcine has provided a new potential use of less useful highly active antioxidant molecule towards the development of oxidative stress related inflammation and its related complication profiles [32].

Antioxidant enriched Siylmarin Nanoparticles

Xia cao et al ventured in developing the porous silica nanoparticles of silymarin to increase the solubility as it has the considerable antioxidant activity. The silymarin nanoparitcles were prepared by porous microemulsion and ultrasonic corrosion methods. The results are bioavailability of silymarin was considerably increased despite the drugs basic poor solubility nature. The evidences are strong that herbal components are appropriate option for oxidative stress management in excessive ROS generation [33].

Metal andioxidant nanoparticle

As antioxidants have significant role in influencing ROS, such antioxidant nanoparticles are prepared from metals such as gold, silver and so on. These methods of producing metal antioxidant nanoparticle using plant extracts are extremely biosynthesized. Kannan et al explored syhthesis of gold nanoparticles using leaf extracts of Coleus amboinicus. The prepared nanoparticles are characterized by UV-vis spectroscopy, XRD, TEM and SAED analyses. This method utilizes cheap production of nanoparticles with non toxic nature {34}. Praveenkumar et al studied gold nanoparticle synthesis using Zingiber officinale extract. They got nanoparticles of size range 5 to 15 nm, and Zingiber officinale as stabilizing and reducing agent which is more potent than asprin. Characterization was done by Dynamic Light scattering (DLS), TEM and UV-Vis Spectroscopy. The produced nanopartcles are biocompatible with the blood has been observed [35].

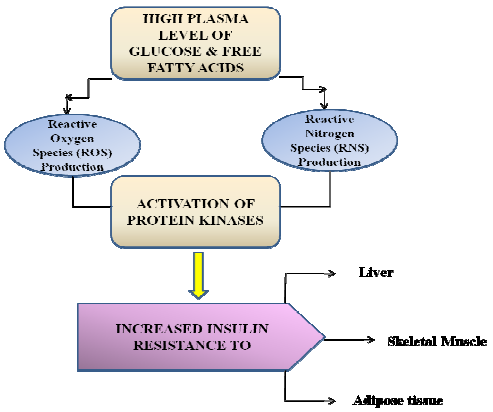

Fig 1: Flow chart showing Insulin Resistance and ROS production

Table 1: List of some herbs for diabetes and its complications

	Botanical name	Common/Vernacular Name
	Eugenia Jambolana	Indian Gooseberry
	Momordica charantia	Bitter gourd
	Ocimum sanctum	Holy Basil
	Phyllanthus amarus	Bhuiawala
	Pterocarpus marsupium	benga
	Tinospora cordifolia	Guduchi
	Trigonella foenum	Fenu greek
	Withania somnifera	Ashwagandha
	Allium sativum	Garlic

Table 2: List of herbs and its intention to intend

Name of Herb	Common/Vernacular	Intention/purpose
Acacia arabica	Babhul	Anti-diabetic agent shown to have hypoglycemic effect.
Aegle marmelos	Bengal Quince	Improves digestion and reduces blood glucose, urea and serum cholesterol level
Allium cepa	Onion	Antioxidant, anti hyperglycemic and anti hyperlipedemic activity
Allium sativum	Garlic	Increases insulin secretion and controls lipid peroxidation
Aloe vera	Kathalai	Stimulates β cell to secrete insulin, Anti-inflammatory and wound healing
Azadirachta indica	Neem	Anti-hyperglycemic, hepatoprotective and antioxidant activity
Eugenia jambolana	Jamun	Anti-hyperglycemic
Mangifera indica	Mango	Anti-diabetic agent, reduces intestinal glucose uptake.
Momordica charantia	Bitter gourd	Antidiabetic and Antihyperglycemic Agent
Ocimum Sanctum	Holy basil	Glucose level decline in fasting condition, triglyceride and total lipid content
Phyllanthus amarus	Bhuiawala	Antiinflammatory, anticancer, antioxidant and antidiarrhoeal

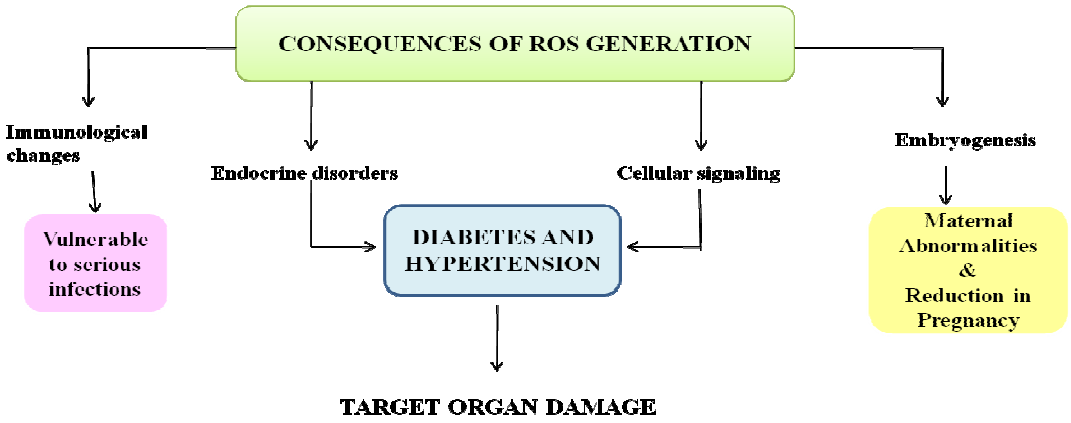

Fig 2: Flow Chart showing Consequences of ROS

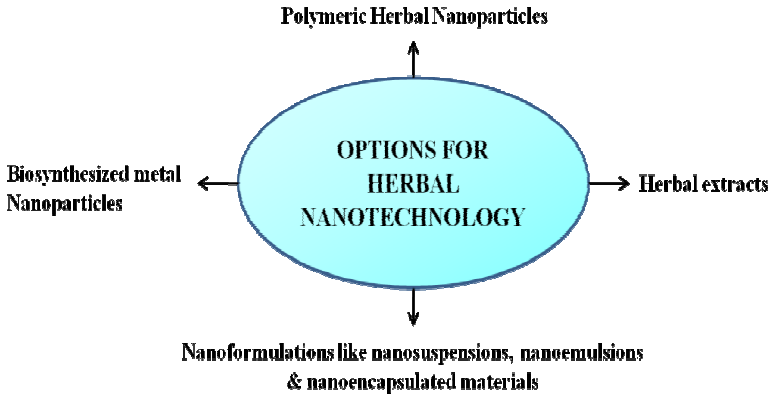

Fig 3: Preference of Herbal Nanotechnology

Conclusion

Diabetic treatment channelizing to the effective control of glucose level and specific strategy to target the ROS generating pathway curbing, do produce better results and compliments each other beneficially. A biological antioxidants capable of restraining oxidative stress mediated diabetic complication in due course of hyperglycemia is still mandatory to foresee better clinical improvements. The antioxidant enriched herbal components is the viable tool to cope with oxidative stress condition in diseased condition especially, the diabetes. Secondly, evidences are there that such components of antioxidant, antidiabetic and hypoglycemic herbs are tailored to nanotization for the maximum benefit. Provided with the strong scientific back up evidences, the clinical implications of nanotechnology based herbal constituents such as antioxidants are in great need to the mankind, to fight with oxidative stress related complications in diabetes and related ailments.

"Cite this article"

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