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OCIMUM SANCTUM AMELIORATE ANTI-OXIDANT, ANTI-MICROBIAL AND IMMUNE SYSTEM FOR THE CONTROL OF DIABETES AGAINST CORONAVIRUS: AN EPISODE

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ABSTRACT

During Novel Corona Virus (COVID 19) pandemic disease patients suffering from more severe outcomes and higher morbidity and mortality in the patients with diabetes. Many events may play a role in this higher morbidity and mortality, especially higher glucose level/hyperglycemia, an impaired immune system, pro-inflammatory condition, microbial susceptibility. Thus the diabetic patients need to know about COVID 19 Pandemic and according to information of 'Ministry of Ayush' Ayurveda's immunity booster may helpful for self-care during COVID 19 crisis. Ocimum sanctum as traditional herbal medicine can play important role in the prevention and treatment of different types of problems related to diabetes. Ocimum sanctum may improve immunity, decrease the reactive oxygen species activity and could defense biological system from viral and microbial infection. During the study, we have collected many articles an overview of the potential role of the Ocimum sanctum during the COVID 19 pandemic for diabetic patients.

KEYWORDS: Coronavirus, Diabetes, Anti-oxidant, Anti-microbial, Immunomodulator.

INTRODUCTION

Viral diseases are the major cause of devastations in human health, virus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. On 31 December 2019, a cluster of pneumonia of unknown etiology was found and identified as COVID-19 virus-infected person suffer from mild to moderate respiratory illness and recover without requiring special treatment.[1] Older people and those with underlying medical problems reported in Wuhan City, Hubei diabetes, chronic respiratory disease, and cancer.[2] A person with such disease is more likely to develop serious illness during the infection period.[3,4] The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes and droplets suspended in the air. COVD-19 virus spread most conveniently by droplet infection (droplet size >5 to 10 µm) from one person to other present nearly 1 m distance during coughing or sneezing reported by WHO. COVID-19 infection announced as pandemic disease and affects millions of people in the world.[5]

American Diabetes Association and Diabetes Canada reported that COVID-19 can cause more severe symptoms and complications in those people suffering from diabetes, the elderly, and persons with additional chronic conditions such as heart disease & lung disease. A diabetic person under medication might be at a higher risk of severe illness from COVID 19. The reason behind this is the immune system does not work effectively as well as in people with diabetes, which makes it harder for their body to fight the virus. Also, the novel coronavirus "may increase in an environment of elevated blood glucose.[6] Diabetes mellitus is a non-infectious endocrine disorder which is characterized by the disturbance in the metabolism of carbohydrate and associated with hyperglycemia.[7,8] It is related to the development of various serious diseases like microvascular (nephropathy and neuropathy) and macrovascular (peripheral vascular disease and coronary heart diseases).[9] Diabetes mellitus is also known as diabetes which was observed as a disease related to sweet urine and muscle loss.

Glucose blood levels are maintained by insulin which is a hormone released from the pancreas. When glucose level increases, insulin is produced from the pancreas and maintained the level of glucose. In a diabetic person, the production of insulin is absent or less which causes hyperglycemia.[10] Diabetes mellitus is three types Type 1, Type 2 and gestational diabetes mellitus. Type 1 Diabetes mellitus is known as insulin-dependent diabetes mellitus (IDDM) which is due to total loss of function of

β cell of islets of Langerhans which are present in the pancreas. Type 2 Diabetes mellitus is known as insulin non-dependent diabetes mellitus (NIDDM) which is the temporary loss of β cell mass and it is due to genetic predisposition and mostly occurs in obese persons and associated with high blood pressure and high cholesterol levels.[11] Type 2 (NIDDM) diabetes is the most common form of the disease in nearly 90 % to 95 % of the cases in which the body does not produce sufficient insulin.[12,13,14] As per World Health Organization the diabetic population will increase up to 300 million or more by the year 2025.[15] Gestational diabetes is a type of diabetes that presents with hyperglycemia in pregnant women.[16,17] The symptoms of diabetes mellitus are polydipsia, polyuria, polyphagia, fatigue, nausea, vomiting, and impotence in men, slow wound healing, and blurred vision.[18]

According to International Diabetes Federation(IDF) survey in 2016 diabetes is a disorder that affects 415 million people in the world and it may increase to 642 million by the year 2040.[19] According to Aroma world reports 61.3 million people to have diabetes in India and consist of 20-79 age groups in the population. It may approx be doubled by the year 2030. Presently India is also known as the diabetes capital of the world and affects mainly rural and urban people of the country.[20] The frequency of diabetes is progressively increasing in urban areas. The frequency of diabetes in an urban area is approx six times more than compared to rural areas.

Decreased exercise, increasing weight, and tension, change in diet, malnutrition, alcohol consumption, viral infection are the major causes of diabetes mellitus in the last 20 years.[21] On the basis of the review study, it is observed that Female diabetic patients are more than compared to male diabetic patients because hormone and inflammation act differently in women. It is also found that people who are less educated have diabetes disorder more than compared to more educated people.[22] The ultimate percentages of people having diabetes are present in developing countries.[23]

The aim of the treatment of diabetes mellitus or especially type 2 is to decrease insulin resistance and increases insulin secretion. The basic reasons for using traditional medicine is that it is more affordable, more closely to the patient's beliefs, dispel concerns about the adverse effects of chemical (synthetic) medicines, natural drug satisfies a desire for more personalized health care, and allows greater public access to health information. Traditional medicine play important role in the prevention and treatment of different types of problem-related to diabetes. India has a superb history in traditional medical therapy. In India, nearly 70% of the population depends on traditional medicine to meet their health care needs.[24,25]

Herbal drugs are useful to the treatment of chronic and acute conditions and various ailments and problems such as cardiovascular disease, prostate problems, depression, inflammation, and to boost the immune system, to name but a few. In China, in 2003, traditional herbal medicines played a prominent role in the strategy to contain and treat severe acute respiratory syndrome (SARS), and in Africa, a traditional herbal medicine, the African flower, has been used for decades to treat wasting symptoms associated with HIV. It is also found that herbal medicines are also very common in Europe, with Germany and France leading in over-the-counter sales among European countries, and in most developed countries, one can find essential oils, herbal extracts, or herbal teas being sold in pharmacies with conventional drugs.[26,27] *Ocimum sanctum* (OS) is one of the most important medicinal plants mentioned in Ayurvedic literature for its medicinal and spiritual properties. The utilization of Tulsi will be a milestone for the diabetic person to improve immunity, defense from viral and microbial infection.

Plant description

Tulsi is a sacred plant of the Hindu religion worshipped all over India? Tulsi means 'incomparable one' or 'matchless one' and is derived from Sanskrit.[28] Also, known as "Queen of Herbs",[29] (incomparable one) (Babita LabhKayastha). *Ocimum sanctum* (Family Labiatae) is a many-branched, erect, plump, and aromatic herb about 55 cm high. This small herb is found all over the world several types of basil are cultivated, some of the widely used varieties can be categorized into two groups – holy basil (*Ocimum sanctum*) and Mediterranean basil (*Ocimum basilicum*) as well in India and is cultivated, worshiped in temples and houses of Hindus.[30]

This is commonly known as Vishnu-Priya, Tulsi in Sanskrit, and Kala Tulsi in Hindi, and India's Holy Basil in English. The leaves, seeds, and roots of this plant have been used in indigenous Ayurvedic medicine. Tulsi plant is traditionally known for its medicinal properties.[31] Tulsi has two verities – Black (Krishna Tulsi) and Green (Ram Tulsi). They have similar chemical and medicinal properties. Genus Ocimum has various species like *Ocimum sanctum* L (Tulsi), *Ocimum. gratissimum* (Ram Tulsi), *Ocimum canum* (Dulal Tulsi), *Ocimum bascilicum* (Ban Tulsi), *Ocimum kilimandschricum*, *Ocimum americanum*, *Ocimum camphora* and *Ocimum micranthum*. Tulsi is also described as Vanya (wild) and Gramya (Grown in homes). The plant is useful in the treatment of cold, cough, dengue, bronchitis, asthma, sore throat, influenza, heart disorders, eye diseases, malaria, mouth infections, insect bites, stress, and kidney stones, etc.[32]

Morphology

It is erect, branched fragmented shrub with a height of about 18 inches when mature. Its leaves are simple, aromatic, branched, opposite, obtuse, elliptical, and have dentate margins. They are up to 5cm long. Flowers are elongate raceme in close whorls and purple in color.

Seeds are radish yellow and fruits are small.[33] It is planted after the rainy season and harvested after few months. Different types of verities are cultivated in different parts of the world and are widely known for their medicinal properties.[34,35] There are 18-types of basil Tulsi, the herb is loved all-over-the world (Table-1).

Types	General Name	Botanical Name	Availability
HOLY Basil			
	Rama tulsi	Ocimum sanctum	India, Eastern Nepal, China, Brazil, and Bangladesh
	Krishna tulsi	Ocimum tenuiflorum	India, Nepal and Bangladesh
	Amrita tulsi	Ocimum tenuiflorum	India, Nepal and Bangladesh
	Vanatulsi	Ocimum gratissimum	India, Nepal and Bangladesh
Mediterranean Basil			
	Sweet basil	Ocimum basilicum	India, Nepal and European countries
	Thai basil	Ocimum thyrsiflora	India, Nepal, south Asia
	Purple basil	Ocimum basilicum	India, Nepal
	Lemon basil	Ocimum citriodorum	Africa, India, Nepal
	Vietnamese basil	Ocimum cinnamon	India ,Nepal
	American basil	Ocimum americanum	India, America, Spain and Egypt
	African blue basil	Ocimum kilimandscharicum	African countries
	Italian genovese basil	ocimum basilicum	Albania, Greece, Turkey, Syria, Lebanon, Israel, Egypt, Libya, Tunisia, Algeria, and Morocco
	Lettuce basil (sweet basil)	ocimum basilicum	India
	Green ruffles basil	ocimum basilicum	America, Mississippi
	Cardinal basil	ocimum basilicum	Japan ,India
	Greek basil	ocimum basilicum	Brazil ,UK
	Spicy globe basil	ocimum basilicum	Thailand and Italy
	Summer long basil	ocimum basilicum	Africa and Japan

Chemical components

Numbers of varieties of compound are available in different parts of Tulsi plant, having important pharmacological role (Table-2).

Types of component	Plant part and active compound	Pharmacological Role	References
Alkaloids	Leaves, stem roots, Eugenol, Luteolin Apigenin	Detoxification analgesic, antispasmodic and bactericidal effects, anti-cancer, anti-oxidant, anti-viral etc	[36]
Glycosides			[37]
Anthraquinone glycosides	Leaves, anthocyans	Laxative effect	[38]
Gums, mucilage	Seed (Sugars) Xylose,polysaccharides	hypoglycemic properties	[39,40]
Proteins&Minerals	Calcium, phosphorous , Iron, Zinc	Enhance nutrition	[41]
Essential Amino acids	Seeds- methionine sulfone, tryptophan	Protein synthesis, Acts as precursor for plant hormones.	[42,43]
Tannins	Leaf, stem Gallic tannins, catecholic tannins	anti-viral, anti-tumor, anti-inflammatory and healing properties on wounds, kidney etc	[44,45]
Phenolic compounds	cirsilineol, circimaritin, isothymusin, apigenin and rosameric acid (Stem),and appreciable quantities of eugenol	Antioxidant Anti-inflammatory Anti-microbial agents.	[46,47]
Steroids			
Flavonoids	Leaves-orientin and vicenin Pentanal (alkyl aldehyde)	Antioxidant, Protects human blood lymphocytes, Anti-cancer	[48,49,50]
Essential oil	Seed (fatty acid, Sitosterol) Leaves - Eugenol, methyl Eugenol, carvacrol, sesquiterpine hydrocarbon caryophyllene	Protection against allergics, inflammation free radicals, platelet aggregation, microbes, ulcers.	[51,52]
fixed oils	Seeds-Oleic acid, Stearic acid,	Antidiabetic Anti-ulcer Anti-arthritic	[53,54]

	Hexourenic acid, Palmitic acid, Linodilinolin and Linolenic acid. Leaves- α‑linolenic acid	activityAnti-pyretic activity	
Terpenes (Sesquiterpenes)	fruits,leaves, flower spikes α–Farnesene	Anti-oxidant, anti-fungal, anti-microbial	[55,56,57]

Pathological risk during diabetes

In a diabetic person with hyperglycemia produce micro and macrovascular complications, during diabetes generation of highly reactive oxygen and nitrogen species.[58] Long term type-2 diabetes mellitus most prevalent form of the disease and represent 90% to 95 % of cases may cause retinopathy, neuropathy, kidney disease, and diabetic neuropathy; short time may cause hypoglycemia with sign and symptoms of rapid heartbeat, sweating, sleepiness, and headaches. Cardiovascular disease (CVD) case nearly 80% deaths in DM patients.[59] Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death word wide and is major health challenges are also related to DM, which acts as a risk factor for HCC.[60] Recently, suggested that all the complications are due to excess generation of highly reactive oxygen and nitrogen species is a key component in the development of complications invoked by hyperglycemia in the diabetes mellitus (DM).[61] Overproduction and/or insufficient removal of these reactive species result in vascular dysfunction, damage to cellular proteins, membrane lipids, and nucleic acids, leading to search for a drug that would be capable of a proper and accurate prevention of the oxidative stress and free radical generation in diabetic patients, especially in the presence of chronic complications. In the face of this scenario, the present review briefly addresses the role of herbal drug Tulsi in hyperglycemia, immunity, antimicrobial, antiviral, and oxidative stress, considering basic mechanisms and their effects in diabetes mellitus, As per American Diabetes Association diabetic persons are two to threefold highly susceptible to COVID 19 infection during an episode of high blood glucose level.[62]

Immunological problem in diabetes

Type1 diabetes is an autoimmune disease or at least has a major autoimmune component causes severe loss of pancreatic β cells.[63] The evidence comes from different sources: the presence of an inflammatory infiltrate (insulitis) in the islets; a strong linkage between type 1 diabetes and certain alleles of the major histocompatibility complex (MHC) 1; and autoantibodies that react with islet cell autoantigens.[64] Loss of pancreatic β cells due to Autoreactive T cells are key mediators of β cell destruction. It is also recorded that Type 2 related to low-grade inflammation (LGI) as a pervasive feature of T2D, accompanying the development and the progression of the disease, as well as the genesis of complications.[65,66,67] Two of the main risk factors to develop T2D are aging and obesity, both known to promote tissue and systemic chronic inflammation often referred to as inflammation and metal inflammation, respectively.[68]

Microbial susceptibility in diabetes

In the study of several researchers it was found that diabetic persons are highly susceptible to infection in joints sepsis and cellulitis potentially increases their morbidity and mortality.[69,70] Data from the experiments support the potential for viral infection in Type -1 diabetic person, epidemiological data show that in Type -1 incidence increase after epidemics due to enterovirus and enteroviral RNA can be detected in the patent.[71] Influenza virus cause limited infection but in individuals who have a pre-existing chronic illness, such as diabetes mellitus, in these individuals, severe influenza can develop.[72] Related to the 2009 H1N1 pandemic, several studies had already suggested that diabetes enhanced the severity of influenza.[73] Valdez et al. (1999) showed that from 1986 to 1989, people with diabetes were more likely to have pneumonia and influenza recorded on their death than people without diabetes.[74]

Pharmacological importance of Tulsi

It is well known that Tulsi has been utilized therapeutically since 4000-5000 BC.[75] The earliest references of Tulsi were found in Rigveda (3500-1600 BC),[76] Therapeutically it is used in anticancer,[77] anti-oxidant, anti-diabetic,[78,79] radiations, infertility, and for many other major and minor diseases,[80] It is good adaptogenic therefore Tulsi is used to improve health,[81,82] Extract of Tulsi is used in Ayurvedic treatments for the common cold, heart diseases, and stomach disorders, poisoning cases, convulsions, epilepsy, malaria, fever, bronchitis, and certain inflammatory problems,[83,84] Therefore, the extract of Tulsi is also known as "Elixir of Life" and considered to endowment long life.

Immunomodulatory Activity

Tulsi is unrivaled in traditional Ayurvedic medicine is a general overall tonic for the immune system.[85] In the double-blind research study in human volunteers increase in the level of interferon- γ and interleukin-4 clearly ascertain the immunomodulatory role of Tulsi,[86] Naturopathic physician Marisa Marciano, MD, wrote in The Naturopathic Herbalist that immunity is a vital component of the interface between individuals and their world. It is an expression of homeostasis and the relationship between bodily health, emotional wellbeing, and mental vision and perspective. Many herbs can stimulate immune responses, and these are best described as immune modulators because they facilitate greater immune system flexibility in the body's natural response to disease. Marciano explained that Tulsi work as immune modulators.[87] Preclinical research in boiler shown immunomodulatory effect Tulsi at the 1% dose level.[88] In research by Rakesh Das et al, all 60 days

study was conducted to evaluate the efficacy of water extract of Ocimum sanctum Linn. leaf on the immune response and disease resistance of Labeo rohita fingerlings against the Aeromonas hydrophila infection. Ocimum sanctum extract was incorporated in the diets (at 0.0%, 0.05%, 0.1%, 0.2%, 0.5% and 1%) of Labeo rohita, rohu fingerlings (6.6, 0.013 g).[89] Several experiments on animal studies have clearly shown immunomodulatory properties in the extract of Tulsi leaves.[90] Dr. D C Mahapatra studied using Tulsi leaf ethanolic (70%) extract in healthy human volunteers through a double-blind randomized controlled trial and found to effective immunomodulatory.[91]

Antimicrobial Activity

The major use of herbal medicines is for health promotion and therapy for chronic, as opposed to life-threatening, conditions. However, usage of traditional remedies increases when conventional medicine is ineffective in the treatment of disease, such as in advanced cancer and in the face of new infectious diseases.[92] Modern research has revealed that the Ocimum sanctum has anti-bacterial, anti-viral, and anti-fungal activity that includes activity against many pathogens responsible for human infections.[93] Ocimum sanctum has also been shown to boost defenses against infective threats by enhancing immune responses in non stressed and stressed animals.[94-95] and healthy humans. While no human trials have been published, there is experimental evidence that Ocimum sanctum may help in the treatment of various human bacterial infections including urinary tract infections,[96] skin and wound infections,[97] typhoid fever,[98] cholera,[99] tuberculosis,[100] gonorrhea,[101] leishmaniasis,[102] various cases of pneumonia,[103] Tulsi's broad-spectrum activity, which includes activity against Streptococcus mutans, the organism responsible for tooth decay, further suggests that it can be used as a herbal mouth wash for treating bad breath, gum disease, and mouth ulcers. This has been confirmed in clinical trials that have demonstrated that rinsing with tulsi is as effective as 0.2% Chlorhexidine and Listerine in reducing the levels of Streptococcus mutants and that a herbal mouthwash that includes tulsi is preferred for its taste and convenience.[104] Tulsi has been tested for its antimicrobial properties against Escherichia coli, Klebsiella, Candida albicans, Staphylococcus aureus, Enterococcus faecalis, and Proteus.[105] Ocimum sanctum demonstrated effectively antimicrobial property against A. actinomycetemcomitans in Periodontitis.[106]

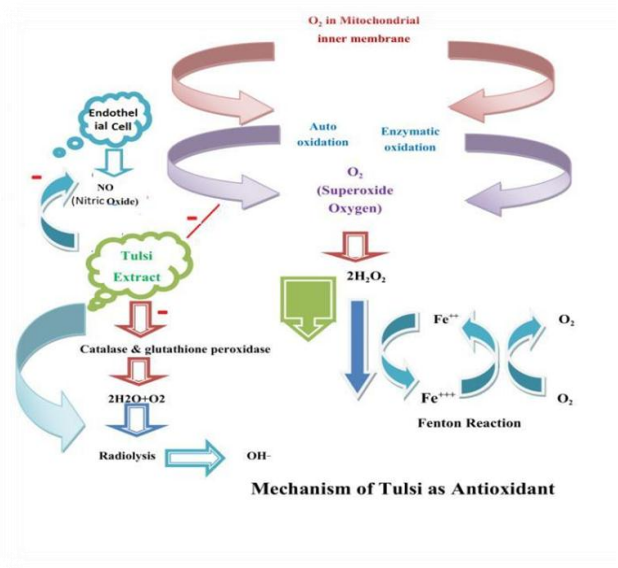
Enterococcus faecalis plays a major role in the etiology of persistent periradicular lesions after root canal treatment and Tulsi was found to be effective in the treatment.[107,108]

In-vito a study showed that there is substantial evidence, suggests that Streptococcus mutants are one of the main culprit microorganisms responsible for dental caries and Tulsi was found to be effective in the treatment. In dental surgery Chlorhexidine is effective against both gram-positive and gram-negative microorganisms since it is a broad-spectrum antimicrobial agent but having unwanted effects like staining of teeth, altered taste, and development of microbial resistance Ocimum sanctum was found effective against Enterococcus faecalis in Endodontics. In-vito study shown that Ocimum sanctum extract is also effective against Streptococcus Mutants and Lactobacillus Acidophilus.[109]

Anti-oxidant activity

In the human body free radicals and other reactive oxygen species are constantly formed, including superoxide anion radical (O^{2-}.), singlet oxygen (O_2), hydrogen peroxide (H_2O_2), and the highly reactive hydroxyl radical (OH) and reactive nitrogen species (RNS).[110] Free-radical activity in the biological cells causes modification of proteins, carbohydrates, DNA, and lipids is a universal mechanism of damage to the cell, especially at the membrane level. It is related to the pathology of several human diseases, including cancer, atherosclerosis, malaria, and rheumatoid arthritis, and neurodegenerative diseases. Free radical plays a central role in aging and in the progression of many diseases and disorders.[111,112]

Antioxidant ingredients of plant source are believed to be the first line of defense against free radical damage and are critical for maintaining optimum health and well-being.[113,114] Many active molecules present in various parts of plants, such as leaves, stem, bark, and roots are now being used in formulations as natural antioxidants for prevention and treatment during various microbial infections in humans.[115] Use of phenolic, flavonoids and terpenes compound of *Ocimum Santum* act as antioxidant and decrease activity of enzymes like catalase, superoxide dismutase, glutathione- S-transferase, which protect cellular components by mopping up damage from free radicals caused by hypoxia and other chemicals.[116,124] (Fig.-1).



Mechanism of Tulsi as Antioxidant

Antiviral activity

Viral infections continue to be a major threat to human population and animal health significance worldwide including India. Infection of viral pathogens, eluding host-viral pathogen and non-availability of the effective antiviral herbal drug has further complicated the therapeutic management of viral diseases in medical practice.[125] Medicinal plants mentioned in Ayurvedic texts have to be evaluated for an antiviral activity for human beings as well as animals. The antiviral drug will have a detrimental effect on the host cellular metabolism posing difficulty in designing drugs acting on specific metabolic pathways of the virus replication only. This has diverted the attention of researchers to develop antiviral agents from their native traditional plant medicine as KrimighnaDravyas.[126-127] Possible antiviral phytochemicals from plant sources like, flavonoids, terpenoids, lignans, sulfides, polyphenolics, coumarins, saponins, furyl compounds, alkaloids, polylines, thiophenes, proteins, and peptides have been reported recently.[128-129] Several important viral pathogens of humans belong to paramyxo and orthmyxo virus family was reported using 10-11 days old embryonated hen's eggs, using aqueous, ethanol, methanol, and chloroform as a solvent, the antiviral effect of Tulsi (*Ocimum sanctum*) crude extracts on similar viruses of veterinary importance were observed, Orthomyxovirus and Paramyxovirus were selected as representative viral agents as they represent an important group of viruses causing economically important and zoonotic diseases of domestic animals and poultry.[130-131]

Infection of Herpes simplex virus (HSV) on the central nervous system, causing meningitis and encephalitis. Viral latency is a problem in the management of HSV treatment. Lethal infections have also been reported in immunocompromised patients. A study by Yucharoen et al represents that plant extracts offer a potential alternative since they are widely used in folklore medicine and they consist of many chemicals for treating disorders or infectious diseases.[132] Synthetic drugs inhibit the DNA polymerase of HSV as per Elion, 1993, it has been used to treat HSV infection. However, the high cost of this synthetic drug means that many patients cannot afford to use it. Furthermore, the development of HSV resistant variants may occur after long-term treatment reported.[133] In the study using African green monkey (GMK) cells line and affect of dichloromethane and methanol solvent extract of various verities of Ocimum sanctum were observed and find effective. In several countries of the Eurasian continent including India in recent years Influenza A viruses (IAVs), members of the family Orthomyxoviridae, avian influenza (AI) H9N2 has become endemic in terrestrial poultry. The spread of AI H9N2 has resulted in significant economic losses in poultry mainly because of reduced egg production and high mortality associated with co-infection with other respiratory pathogens. In the study by R. Sood et all using the embryonated chicken effect of hydro-methanol (1:1 dilution with water) extracts of two plants leaves Ocimum sanctum and A. arabica were prepared and found to highly effective against the H9N2 virus.[134] In the research work of Lien-Chai Chiang *et all Ocimum basilicum* was found to be effective against DNA viruses (herpes viruses -HSV, adenoviruses -ADV and hepatitis B virus) and RNA viruses (coxsackievirus B1 -CVB1 and enterovirus 71 -EV71).[135]

Antidiabetic Activity

Presently insulin and many oral Antidiabetic drugs are available but many of these having may serious side effect; therefore herbal drug *Ocimum sanctum* may play important role as effective Antidiabetic drug as studies by many researchers and reviewer.[136-137] Different parts of the plant including areal leaves, flower, seeds, branches and remaining plant play important which acts as insulinomimetic or secretagogues property and with low economic cost.[138-139] Recently many researchers and reviewers report about *Ocimum sanctum* as traditional medicine used worldwide from ancient time reported in Ayurveda as "elixir of life" and well known for its medicinal, nutritional and spiritual properties. Significant effects have been studied in many scientific reports including preclinical and clinical studies.[140-142] These studies found that Tulsi has unique medicinal effects that include antiinflammatory, antipyretic, antiallergic, antiasthmatic, antitussive, antiulcer, antiemetic, antispasmodic, mosquito repellent, anti-diarrheal, anti-stress, hepato-protective, cardio-protective, neuroprotective, anti-hypercholesterolemia, anti-coagulant activity, adaptogenic, antithyroid, anti-cataract, anti-carcinogenic, radioprotective, anti-hypertensive, analgesic, CNS depressant, memory enhancement, diaphoretic, antifertility, anti-ulcer, anti-leucodermal, antimicrobial (includes antifungal, antiprotozoal, antimalarial, antihelminthic), anti-arthritic, anti-toxic, wound heal effect.[143] Many active constituents present in the *Ocimum sanctum* responsible for Antidiabetic activity. Tulsi has also to be observed to reduce insulin resistance in type-2 diabetes and also improve the lipid profile and decrease triglyceride level, increase insulin release from cells.[144-145] It is well known that long term diabetic person suffer with vascular complication as well as cardiovascular disease and acts as a risk factor and cause 70% death of diabetic persons. A person with high body mass index (BMI) or obesity having a high risk of Type-2 diabetes if a person uses *Ocimum sanctum* as a dietary supplement having anti-diabetic effect.[146]

METHODOLOGY

We have exhaustively reviewed many published literature on recent developments in research of Osmium sanctum, including Online published articles, published in books, theses, conference proceedings, and papers as secondary data from various search engine such as Pubmed, Pubmed Central Databases, Google Scholar, Crossref, WorldCat, Harvard library, Mendeley, Scilit, Cite factor, Shodhganga, Science Central, AYUSH

Research Portal, Open J-Gate, Biblioteca were explored for data collection and report. Pharmacological importance and the effects of Osmium sanctums observed with different experiments were collected for the review purpose.

CONCLUSION

The aim of the present study to provide information on COVID 19 pandemics to diabetic patients its complications and the use of *Ocimum sanctum*. During this worldwide pandemic, diabetic persons under medication might be at high risk. Use of traditional herbal medicine *Ocimum sanctum* during COVID 19 pandemics can reduce pathological risk of a diabetic patient, *Ocimum sanctum* acts as a tonic for immune system, anti-bacterial, anti-viral, anti-fungal as well as antidiabetic during a research study. The use of Ocimum sanctum in diabetic patients can reduce diabetic risk during the critical period of COVID 19 pandemics duration and *Ocimum sanctum* may be used to improve diabetic status. Thus, in this context further there is a high need of screening to find out the marker compound so that a mechanism of action may be established against coronavirus for future management of diabetes like severe metabolic disorder.

REFERENCES

1. Yang P, Wang X. COVID-19: a new challenge for human beings. Cellular & molecular immunology, 2020; 17(5): 555-7.
2. Li H, Yang L, Liu FF, Ma XN, He PL, Tang W, Tong XK, Zuo JP. Overview of therapeutic drug research for COVID-19 in China. Acta Pharmacologica Sinica, 2020; 41(9):1133-40.
3. Noh J, Chang HH, Jeong IK, Yoon KH. Coronavirus disease 2019 and diabetes: the epidemic and the Korean Diabetes Association perspective. Diabetes & metabolism journal, 2020; 44(3): 372-81.
4. Chung SM, Lee YY, Ha E, Yoon JS, Won KC, Lee HW, Hur J, Hong KS, Jang JG, Jin HJ, Choi EY. The risk of diabetes on clinical outcomes in patients with coronavirus disease 2019: a retrospective cohort study. Diabetes & metabolism journal, 2020 May 21; 44(3): 405-13.
5. Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health, 2020; 25(3): 278.
6. Mackenzie SC, Cumming KM, Garrell D, Brodie D, Wilson L, Mehar S, Cunningham SG, Bickerton A, Wake DJ. Massive open online course for type 2 diabetes self-management: adapting education in the COVID-19 era. BMJ Innovations, 2021; 7(1).
7. Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues. The Australasian medical journal, 2013; 6(10): 524.
8. Rahimi M. A Review: Anti Diabetic medicinal plants used for diabetes mellitus. Bulletin of environmental, pharma-cology and life. Sciences, 2015; (4): 163–180.
9. Rao MU. Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty CM. Herbal Medicines for Diabetes Mellitus. A ReviewIn-ternational Journal of PharmTech Research, 2010; (2): 1883– 1892.
10. Bordoloi R, Dutta KN. A review on herbs used in the treatment of diabetes mellitus. J Pharm Chem Biol Sci., 2014; 2(2): 86-92.
11. Wannes WA, Marzouk B. Research progress of Tunisian medicinal plants used for acute diabetes. Journal of Acute Disease, 2016; 5(5): 357–363.
12. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes research and clinical practice, 2010; 87(1): 4-14.
13. Boyle JP, Engelgau MM, Thompson TJ, Goldschmid MG, Beckles GL, Timberlake DS, Herman WH, Ziemer DC, Gallina DL. Estimating prevalence of type 1 and type 2 diabetes in a population of African Americans with diabetes mellitus. American Journal of Epidemiology, 1999; 149(1): 55-63.
14. Cicero L, Yenshou L, Arlene PB, Yi-Ching C, Shao-Chih C, Wen-Chin Y. Herbal therapies for type 2 diabetes mellitus: Chemistry, biology, and potential application of selected plants and compounds. Evidence-based Comp Alt Med, 2013; 33-6.
15. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2020; 14(4): 303-10.
16. Wannes WA, Marzouk B. Research progress of Tunisian medicinal plants used for acute diabetes. Journal of Acute Disease, 2016; 5(5): 357–363.
17. Vijay Patel and Meena Joshi, Antidiabetic Activity Of Aqueous Extract Of Caesalpinia Bonducella Leaves In Streptozotocin Induced Diabetic Rats, European Journal Of Pharmaceutical And Medical Research, 2020; 7(2): 362-367.
18. De Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosomatic medicine, 2001; 63(4): 619-30.
19. Verma S, Gupta M, Popli H, Aggarwal G. Diabetes mellitus treatment using herbal drugs. International Journal of Phytomedicine, 2018; 10(1): 1-0.
20. Ozkum D. Akı O, Toklu HZ. Herbal medicine use among diabetes mellitus patients in Northern Cyprus. Journal of Medicinal Plants Research, 2013; (7): 1652–1664.
21. Narayan DS, Patra VJ, Dinda SC. Diabetes and Indian traditional medicines: an overview. Int J Pharm Pharm Sci., 2012; 4(3): 45-53.
22. Chaudhary Muhammad Junaid Nazar1, MichealMauton Bojerenu2, Muhammad Safdar1, Jibran Marwat1, Effectiveness of diabetes education and awareness of diabetes mellitus in

combating diabetes in the United Kigdom; a literature review, Journal of Nephropharmacology, 2016; 5(2): 110–115.
23. Animaw W, Seyoum Y. Increasing prevalence of diabetes mellitus in a developing country and its related factors. PloS one, 2017; 12(11): e0187670.
24. Pandey MM, Rastogi S, Rawat AK. Indian traditional ayurvedic system of medicine and nutritional supplementation. Evidence-Based Complementary and Alternative Medicine, 2013.
25. Saikat Sen and Raja Chakraborty, "Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: Importance, challenges and future" J Tradit Complement Med, 2017; 7(2): 234–244.
26. Wachtel-Galor S, Benzie IF. 1 Herbal Medicine. Lester Packer, 2011; 28: 1.
27. Shahrajabian MH, Sun W, Shen H, Cheng Q. Chinese herbal medicine for SARS and SARS-CoV-2 treatment and prevention, encouraging using herbal medicine for COVID-19 outbreak. Acta Agriculturae Scandinavica, Section B—Soil & Plant Science, 2020; 70(5): 437-43.
28. Kaushik Vilas Kulkarni and Dr. BelvotagiVenkatraoAdavirao, A review on: Indian traditional shrub Tulsi (ocimum sanctum): The unique medicinal plant, Journal of Medicinal Plants Studies, 2018; 6(2): 106-110.
29. Kaushik R, Gupta D, Yadav R. Alopecia: herbal remedies. International Journal of Pharmaceutical Sciences and Research, 2011 Jul; 2(7): 1631.
30. Mousavi L, Salleh RM, Murugaiyah V. Phytochemical and bioactive compounds identification of Ocimum tenuiflorum leaves of methanol extract and its fraction with an anti-diabetic potential. International Journal of Food Properties, 2018; 21(1): 2390-9.
31. Pandey G, Madhuri S. Pharmacological activities of Ocimum sanctum (tulsi): a review. Int J Pharm Sci Rev Res., 2010; 5(1): 61-6.
32. Baby Joseph and Vrundha M. Nair, "Ethanopharmacological and Phytochemical Aspects of Ocimum sanctum Linn- The Elixir of Life" British Journal of Pharmaceutical Research, 2013; 3(2): 273-292.
33. Kumar PK, Kumar MR, Kavitha K, Singh J, Khan R. Pharmacological actions of Ocimum sanctum–review article. International Journal of Advances in Pharmacy, Biology and Chemistry, 2012; 1(3): 2277-4688.
34. Buddhadev SG, Buddhadev SS, Mehta ND. A review article on Ocimum Sanctum Linn. Int. Peer Revd. Ayur. J., 2014; 2(2): 1-6.
35. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. Journal of clinical biochemistry and nutrition, 2007; 40(3): 163-73.
36. Prakash P, Gupta N. Therapeutic uses of Ocimum sanctum Linn. Tulsi with a note on eugenol and its pharmacological actions:A short review. Indian J Physiol Pharmacol, 2005; 49: 125-31.
37. Borah R, Biswas SP. Tulsi (Ocimum sanctum), excellent source of phytochemicals. International Journal of Environment, Agriculture and Biotechnology, 2018; 3(5): 265258.
38. Han F, Chen YH, Zhou YW, Xu BC. Synthesis and characterization of glycoside-based trisiloxane surfactant. Journal of Surfactants and Detergents, 2011; 14(4): 515-20.
39. Nwankwo CH, Nandy B, Nwankwo BO. Factors influencing diabetes management outcome among patients attending government health facilities in South East, Nigeria. International journal of tropical medicine, 2010; 5(2): 28-36.
40. Khosla MK. Sacred tulsi (Ocimum sanctum L.) in traditional medicine and pharmacology. Ancient science of life, 1995; 15(1): 53.
41. Pattanayak P, Behera P, Das D, Panda SK. Ocimum sanctum Linn. A reservoir plant for therapeutic applications: An overview. Pharmacognosy reviews, 2010; 4(7): 95. 42.
42. Ziemichód A, Wójcik M, Różyło R. Ocimum tenuiflorum seeds and Salvia hispanica seeds: mineral and amino acid composition, physical properties, and use in gluten-free bread. CyTA-Journal of Food, 2019; 17(1): 804-13.
43. Sankhalkar S, Vernekar V. Quantitative and Qualitative analysis of Phenolic and Flavonoid content in Moringa oleifera Lam and Ocimum tenuiflorum L. Pharmacognosy research, 2016; 8(1): 16.
44. Nagaraju N, Rao KN. A survey of plant crude drugs of Rayalaseema, Andhra Pradesh, India. Journal of Ethnopharmacology, 1990; 29(2): 137-58.
45. Joshi B, Sah GP, Basnet BB, Bhatt MR, Sharma D, Subedi K, Janardhan P, Malla R. Phytochemical extraction and antimicrobial properties of different medicinal plants: Ocimum sanctum (Tulsi), Eugenia caryophyllata (Clove), Achyranthes bidentata (Datiwan) and Azadirachta indica (Neem). Journal of Microbiology and Antimicrobials, 2011; 3(1): 1-7.
46. Ahmed AF, Attia FA, Liu Z, Li C, Wei J, Kang W. Antioxidant activity and total phenolic content of essential oils and extracts of sweet basil (Ocimum basilicum L.) plants. Food Science and Human Wellness, 2019; 8(3): 299-305.
47. Borah A, Paw M, Gogoi R, Loying R, Sarma N, Munda S, Pandey SK, Lal M. Chemical composition, antioxidant, anti-inflammatory, anti-microbial and in-vitro cytotoxic efficacy of essential oil of Curcuma caesia Roxb. leaves: An endangered medicinal plant of North East India. Industrial crops and products, 2019; 129: 448-54.
48. Loying R, Gogoi R, Sarma N, Borah A, Munda S, Pandey SK, Lal M. Chemical compositions, in-vitro antioxidant, anti-microbial, anti-inflammatory and cytotoxic activities of essential oil of Acorus

calamus L. rhizome from North-East India. Journal of Essential Oil Bearing Plants, 2019; 22(5): 1299-312.
49. Gogoi R, Loying R, Sarma N, Munda S, Pandey SK, Lal M. A comparative study on antioxidant, anti-inflammatory, genotoxicity, anti-microbial activities and chemical composition of fruit and leaf essential oils of Litsea cubeba Pers from North-east India. Industrial Crops and Products, 2018; 125: 131-9.
50. Joshi S, Karna AK. Analysis of phytoconstiuents and cytotoxic activities of different parts of Ocimum sanctum. International Journal of Applied Sciences and Biotechnology, 2013; 1(3): 137-44.
51. Hussain AI, Chatha SA, Kamal GM, Ali MA, Hanif MA, Lazhari MI. Chemical composition and biological activities of essential oil and extracts from Ocimum sanctum. International Journal of food properties, 2017; 20(7): 1569-81.
52. Siva M, Shanmugam KR, Shanmugam B, Venkata SG, Ravi S, Sathyavelu RK, Mallikarjuna K. Ocimum sanctum: a review on the pharmacological properties. Int. J. Basic Clin. Pharmacol, 2016; 5: 558-65.
53. Suanarunsawat T, Anantasomboon G, Piewbang C. Anti-diabetic and anti-oxidative activity of fixed oil extracted from Ocimum sanctum L. leaves in diabetic rats. Experimental and therapeutic medicine, 2016; 11(3): 832-40.
54. Parasuraman S, Balamurugan S, Christapher PV, Petchi RR, Yeng WY, Sujithra J, Vijaya C. Evaluation of antidiabetic and antihyperlipidemic effects of hydroalcoholic extract of leaves of Ocimum tenuiflorum (Lamiaceae) and prediction of biological activity of its phytoconstituents. Pharmacognosy research, 2015; 7(2): 156.
55. Huelin FE, Murray KE. α-Farnesene in the natural coating of apples. Nature, 1966; 210(5042): 1260-1.
56. Yamani HA, Pang EC, Mantri N, Deighton MA. Antimicrobial activity of Tulsi (Ocimum tenuiflorum) essential oil and their major constituents against three species of bacteria. Frontiers in microbiology, 2016; 7: 681.
57. Çelik K, Toğar B, Türkez H, Taşpinar N. In vitro cytotoxic, genotoxic, and oxidative effects of acyclic sesquiterpene farnesene. Turkish Journal of Biology, 2014; 38(2): 253-9.
58. Son SM. Reactive oxygen and nitrogen species in pathogenesis of vascular complications of diabetes. Diabetes & metabolism journal, 2012; 36(3): 190.
59. Bandeira DM, Da Fonseca LJ, Guedes DS, Rabelo LA, Goulart MO, Vasconcelos SM. Oxidative stress as an underlying contributor in the development of chronic complications in diabetes mellitus. International journal of molecular sciences, 2013; 14(2): 3265-84.
60. Chun Gao, Molecular pathological epidemiology in diabetes mellitus and risk of hepatocellular carcinoma, World J Hepatol, 2016; 8(27): 1119-1127.
61. Yan AF, Sun X, Zheng J, Mi B, Zuo H, Ruan G, Hussain A, Wang Y, Shi Z. Perceived risk, behavior changes and Health-related outcomes during COVID-19 pandemic: Findings among adults with and without diabetes in China. Diabetes research and clinical practice, 2020; 167: 108350.
62. Joensen LE, Madsen KP, Holm L, Nielsen KA, Rod MH, Petersen AA, Rod NH, Willaing I. Diabetes and COVID-19: psychosocial consequences of the COVID-19 pandemic in people with diabetes in Denmark—what characterizes people with high levels of COVID-19-related worries?. Diabetic Medicine, 2020; 37(7): 1146-54.
63. Alberto Pugliese: Autoreactive T cells in type 1 diabetes, J Clin Invest, 2017; 127(8): 2881-2891.
64. Zóka A, Műzes G, Somogyi A, Varga T, Szémán B, Al-Aissa Z, Hadarits O, Firneisz G. Altered immune regulation in type 1 diabetes. Clinical and Developmental Immunology, 2013.
65. Itariu BK, Stulnig TM. Autoimmune aspects of type 2 diabetes mellitus-a mini-review. Gerontology, 2014; 60(3): 189-96.
66. Pitsavos C, Tampourlou M, Panagiotakos DB, Skoumas Y, Chrysohoou C, Nomikos T, Stefanadis C. Association between low-grade systemic inflammation and type 2 diabetes mellitus among men and women from the ATTICA study. The review of diabetic studies: RDS. 2007; 4(2): 98.
67. Van Greevenbroek MM, Schalkwijk CG, Stehouwer CD. Obesity-associated low-grade inflammation in type 2 diabetes mellitus: causes and consequences. Neth J Med, 2013; 71(4): 174-87.
68. JuhuaLuo , Allison Hodge, Michael Hendryx, Julie E. Byles: Age of obesity onset, cumulative obesity exposure over early adulthood and risk of type 2 diabetes, Diabetologia, 2020; 63: 519–527.
69. Anton Y. Peleg,ThilakWeerarathna, James S. McCarthy, Timothy M. E. Davis: Common infections in diabetes: pathogenesis, management and relationship to glycaemic control, Diabetes Metab Res Rev., 2007; 23: 3–13.
70. Frydrych LM, Fattahi F, He K, Ward PA, Delano MJ. Diabetes and sepsis: risk, recurrence, and ruination. Frontiers in endocrinology, 2017; 8: 271.
71. Urs Christena, Christine Bendera, and Matthias G. von Herrathba; Infection as a cause of type 1 diabetes? Curr Opin Rheumatol, 2012; 24(4): 417–423.
72. Daniel J. Drucker; Coronavirus Infections and Type 2 Diabetes-Shared Pathways with Therapeutic Implications, Endocrine Reviews, 2020; 41(3): 457–469
73. Hulme KD, Gallo LA, Short KR. Influenza virus and glycemic variability in diabetes: a killer combination?. Frontiers in microbiology, 2017; 8: 861.

74. Valdez R, Narayan KM, Geiss LS, Engelgau MM. Impact of diabetes mellitus on mortality associated with pneumonia and influenza among non-Hispanic black and white US adults. American Journal of Public Health, 1999; 89(11): 1715-21.
75. Tewari D, Sah AN, Pandey HK, Meena HS, Meena R, Ramaswamy RS, Reddy RC, Deo YK, Bandari S, Bhadra DP, Murthy PH. A review on phytoconstituents of Ocimum (Tulsi). International Journal of Ayurvedic Medicine, 2012; 3(1): 1-9.
76. Prakash PA, Gupta N. Therapeutic uses of Ocimum sanctum Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian journal of physiology and pharmacology, 2005; 49(2): 125.
77. Baliga MS, Jimmy R, Thilakchand KR, Sunitha V, Bhat NR, Saldanha E, Rao S, Rao P, Arora R, Palatty PL. Ocimum sanctum L (Holy Basil or Tulsi) and its phytochemicals in the prevention and treatment of cancer. Nutrition and cancer, 2013; 65(sup1): 26-35.
78. Gupta S, Mediratta PK, Singh S, Sharma KK, Shukla R. Antidiabetic, antihypercholesterolaemic and antioxidant effect of Ocimum sanctum (Linn) seed oil. Indian Journal of Experimental Biology, (44): 206-300-304.
79. Khan MR, Islam MA, Hossain MS, Asadujjaman M, Wahed MI, Rahman BM, Anisuzzaman AS, Shaheen SM, Ahmed M. Antidiabetic effects of the different fractions of ethanolic extracts of Ocimum sanctum in normal and alloxan induced diabetic rats. Journal of Scientific Research, 2010; 2(1): 158-68.
80. Sethi J, Yadav M, Sood S, Dahiya K, Singh V. Effect of tulsi (Ocimum Sanctum Linn.) on sperm count and reproductive hormones in male albino rabbits. International journal of Ayurveda research, 2010; 1(4): 208.
81. Jamshidi N, Cohen MM. The clinical efficacy and safety of Tulsi in humans: a systematic review of the literature. Evidence-Based Complementary and Alternative Medicine, 2017.
82. Patwardhan B, Gautam M. Botanical immunodrugs: scope and opportunities. Drug discovery today, 2005; 10(7): 495-502.
83. Subir Kumar Das and D M Vasudevan; Tulsi: The Indian holy power plant, Natural Product Radiance, 2006; 5(4): 279-283.
84. Bilal A, Jahan N, Ahmed A, Bilal SN, Habib S, Hajra S. Phytochemical and pharmacological studies on Ocimum basilicum Linn-A review. International Journal of Current Research and Review, 2012; 4(23).
85. Kumar A, Rahal A, Chakraborty S, Tiwari R, Latheef SK, Dhama K. Ocimum sanctum (Tulsi): a miracle herb and boon to medical science–A Review. Int J Agron Plant Prod, 2013; 4(7): 1580-9.
86. Shankar Mondala, Saurabh Varmab, Vishwa Deepak Bamolaa, Satya Narayan Naikc, Bijay Ranjan Mirdhad, Madan Mohan Padhie, NalinMehtaa, Sushil Chandra Mahapatraa;Double-blinded randomized controlled trial for immunomodulatory effects of Tulsi (Ocimum sanctum Linn.) leaf extract on healthy volunteers,Journal of Ethnopharmacology, 2011; 136: 452– 456.
87. Reddy ET, Reddy PS, Ramya P, Kumari KN. Effect of supplementation of amla, tulsi and turmeric on bio-chemical parameters and immune responses in broilers. Indian Journal of Poultry Science, 2012; 47(1): 114-7.
88. Singh A, Doley P. Immunomodulatory Effect of Tulsi (Ocimum Sanctum) Leaves Powder Supplemented in Broilers. International Journal of Science and Research, 3(8).
89. Das R, Raman RP, Saha H, Singh R. Effect of Ocimum sanctum Linn.(Tulsi) extract on the immunity and survival of Labeo rohita (Hamilton) infected with Aeromonas hydrophila. Aquaculture Research, 2015; 46(5): 1111-21.
90. Das BD, Mishra RK, Kumar A, Kumari R, Das V, Paudel N, Choudhary SK. Assessment of Surface Water Quality by Using Water Quality Index of Sanbarish Pond of Morang District, Nepal. American Scientific Research Journal for Engineering, Technology, and Sciences (ASRJETS), 2020; 63(1): 137-43.
91. Mahapatra S. Immunomodulatory effects of Tulsi (Ocimum sanctum linn.) on healthy human subjects. Department Of Physiology, AIIMS, New Delhi, 2011; 110029.
92. Wachtel-Galor S, Benzie IF. Herbal medicine: biomolecular and clinical aspects. 2nd edition. Boca Raton (FL): CRC Press/Taylor &Francis, 2011.
93. Anand K, Tiloke C, Naidoo P, Chuturgoon AA. Phytonanotherapy for management of diabetes using green synthesis nanoparticles. Journal of Photochemistry and Photobiology B: Biology, 2017; 173: 626-39.
94. Hemalatha R, Babu KN, Karthik M, Ramesh R, Kumar BD, Kumar PU. Immunomodulatory activity and Th1/Th2 cytokine response of Ocimum sanctum in myelosuppressed swiss albino mice. Trends Med Res., 2011; 6: 23-31.
95. Pavaraj M, Balasubramanian V, Baskaran S, Ramasamy P. Development of immunity by extract of medicinal plant. Ocimum sanctum. 2011; 4(1): 12-18.
96. Ali H, Dixit S. In vitro antimicrobial activity of flavanoids of Ocimum sanctum with synergistic effect of their combined form. Asian Pacific Journal of Tropical Disease, 2012; 2: S396-8.
97. Goel A, Kumar S, Singh DK, Bhatia AK. Wound healing potential of Ocimum sanctum Linn. with induction of tumor necrosis factor. Indian Journal of Experimental Biology, 2010; 48: 402-406.
98. Joshi B, Sah GP, Basnet BB, Bhatt MR, Sharma D, Subedi K, Janardhan P, Malla R. Phytochemical

extraction and antimicrobial properties of different medicinal plants: Ocimum sanctum (Tulsi), Eugenia caryophyllata (Clove), Achyranthes bidentata (Datiwan) and Azadirachta indica (Neem). Journal of Microbiology and Antimicrobials, 2011; 3(1): 1-7.
99. Kumar KP, Bhowmik D, Tripathi KK, Chandira M. Traditional Indian Herbal Plants Tulsi and Its Medicinal Importance. Research Journal of Pharmacognosy and Phytochemistry, 2010; 2(2): 93-101.
100. Pavithra N, Sathish L, Ananda K. Antimicrobial and enzyme activity of endophytic fungi isolated from Tulsi. Journal of Pharmaceutical and Biomedical Sciences (JPBMS), 2012; 16(16): 2014.
101. Shokeen P, Bala M, Singh M, Tandon V. In vitro activity of eugenol, an active component from Ocimum sanctum, against multiresistant and susceptible strains of Neisseria gonorrhoeae. International journal of antimicrobial agents, 2008; 32(2): 174-9.
102. Suzuki A, Shirota O, Mori K, Sekita S, Fuchino H, Takano A, Kuroyanagi M. Leishmanicidal active constituents from Nepalese medicinal plant Tulsi (Ocimum sanctum L.). Chemical and Pharmaceutical Bulletin, 2009; 57(3): 245-51.
103. Durga KR, Karthikumar S, Jegatheesan K. Isolation of potential antibacterial and antioxidant compounds from Acalypha indica and Ocimum basilicum. Journal of Medicinal Plants Research, 2009; 3(10): 703-6.
104. Agarwal P, Nagesh L. Evaluation of the antimicrobial activity of various concentrations of Tulsi (Ocimum sanctum) extract against Streptococcus mutans: an in vitro study. Indian Journal of Dental Research, 2010; 21(3).
105. Ballal M. Activity of Ocimum sanctum (the traditional Indian medicinal plant) against the enteric pathogens. Indian journal of medical sciences, 2001; 55(8): 434-8.
106. Mallikarjun S, Rao A, Rajesh G, Shenoy R, Pai M. Antimicrobial efficacy of Tulsi leaf (Ocimum sanctum) extract on periodontal pathogens: An in vitro study. Journal of Indian Society of Periodontology, 2016; 20(2): 145.
107. Chandrappa PM, Dupper A, Tripathi P, Arroju R, Sharma P, Sulochana K. Antimicrobial activity of herbal medicines (tulsi extract, neem extract) and chlorhexidine against Enterococcus faecalis in Endodontics: An in vitro study. Journal of International Society of Preventive & Community Dentistry, 2015; 5(Suppl 2): S89.
108. Subbiya A, Mahalakshmi K, Pushpangadan S, Padmavathy K, Vivekanandan P, Sukumaran VG. Antibacterial efficacy of Mangifera indica L. kernel and Ocimum sanctum L. leaves against Enterococcus faecalis dentinal biofilm. Journal of conservative dentistry: JCD, 2013; 16(5): 454.
109. Shah S, Trivedi B, Patel J, Dave JH, Sathvara N, Shah V. Evaluation And Comparison Of Antimicrobial Activity Of Tulsi (Ocimum Sanctum) Neem (Azadirachta Indica) And Triphala Extract Against Streptococcus Mutans&Lactobacillus Acidophilus: An In Vitro Study. National Journal of Integrated Research in Medicine, 2014; 5(4).
110. Riley PA. Free radicals in biology: oxidative stress and the effects of ionizing radiation. International journal of radiation biology, 1994; 65(1): 27-33.
111. Phaniendra A, Jestadi DB, Periyasamy L. Free radicals: properties, sources, targets, and their implication in various diseases. Indian journal of clinical biochemistry, 2015; 30(1): 11-26.
112. Aruoma OI. Free radicals, oxidative stress, and antioxidants in human health and disease. Journal of the American oil chemists' society, 1998; 75(2): 199-212.
113. Sumran G, Aggarwal A. Prospect of Indian herbs as sources of antioxidants in combating oxidative stress. Chemistry & Biology Interface, 2019; 9(1).
114. Young IS, Woodside JV. Antioxidants in health and disease. Journal of clinical pathology, 2001; 54(3): 176-86.
115. Katalinic V, Milos M, Kulisic T, Jukic M. Screening of 70 medicinal plant extracts for antioxidant capacity and total phenols. Food chemistry, 2006; 94(4): 550-7.
116. Ighodaro OM, Akinloye OA. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. Alexandria journal of medicine, 2018; 54(4): 287-93.
117. Jeeva JS, Sunitha J, Ananthalakshmi R, Rajkumari S, Ramesh M, Krishnan R. Enzymatic antioxidants and its role in oral diseases. Journal of pharmacy & bioallied sciences, 2015; 7(Suppl 2): S331.
118. Banjarnahor SD, Artanti N. Antioxidant properties of flavonoids. Medical Journal of Indonesia, 2014; 23(4): 239-44.
119. Catapano AL. Antioxidant effect of flavonoids. Angiology, 1997 Jan; 48(1): 39-44.
120. Urquiaga IN, Leighton F. Plant polyphenol antioxidants and oxidative stress. Biological research, 2000; 33(2): 55-64.
121. Catapano AL. Antioxidant effect of flavonoids. Angiology, 1997; 48(1): 39-44.
122. Yanpallewar SU, Rai S, Kumar M, Acharya SB. Evaluation of antioxidant and neuroprotective effect of Ocimum sanctum on transient cerebral ischemia and long-term cerebral hypoperfusion. Pharmacology Biochemistry and Behavior, 2004; 79(1): 155-64.
123. Agarwal K, Singh DK, Jyotshna J, Ahmad A, Shanker K, Tandon S, Luqman S. Antioxidative potential of two chemically characterized Ocimum (Tulsi) species extracts. Biomedical Research and Therapy, 2017; 4(9): 1574-90.

124. Sundaram RS, Ramanathan M, Gowtham L, Jena PK, Choudhury GB, Manikandan P, Venugopal V, Kamalakannan D. Investigation of Standardized Ethanolic Extract of Ocimum sanctum Linn.(Holy Basil) Leaves for its in vitro Antioxidant Potential and Phenolic Composition. Asian Journal of Chemistry, 2012; 24(4).
125. Alcorn SR. The 2020 Coronavirus (COVID-19) Global Pandemic, a Call to Arms to Pharmacognosy Researchers-Plant-Based Antiviral Approaches. Pharmacognosy Communications, 2021; 11(1).
126. Rathi B, Rathi R, Khobragade P. Relevance of Ayurveda Anti-viral herbal wisdom from the perspective of current researches. International Journal of Research in Pharmaceutical Sciences, 2020; 11(Special Issue 1).
127. Sen B. Potentiality and possibility of Medicinal Plants on Ayurvedic Principle in prevention and treatment of COVID-19. J Ayurvedic Herb Med, 2020; 6: 100-7.
128. Jassim SA, Naji MA. Novel antiviral agents: a medicinal plant perspective. Journal of applied microbiology, 2003; 95(3): 412-27.
129. Kapoor R, Sharma B, Kanwar SS. Antiviral phytochemicals: an overview. Biochem Physiol, 2017; 6(2): 7.
130. Patil U. Studies on antiviral activity of tulsi (Ocimum sanctum) crude extracts on selected viruses of veterinary importance. International Journal of Ayurveda and Pharma Research, 2018; 6(4).
131. Ghoke SS, Sood R, Kumar N, Pateriya AK, Bhatia S, Mishra A, Dixit R, Singh VK, Desai DN, Kulkarni DD, Dimri U. Evaluation of antiviral activity of Ocimum sanctum and Acacia arabica leaves extracts against H9N2 virus using embryonated chicken egg model. BMC complementary and alternative medicine, 2018; 18(1): 1-0.
132. Yucharoen R, Anuchapreeda S, Tragoolpua Y. Anti-herpes simplex virus activity of extracts from the culinary herbs Ocimum sanctum L., Ocimum basilicum L. and Ocimum americanum L. African Journal of Biotechnology, 2011; 10(5): 860-6.
133. Crumpacker CS, Schnipper LE, Marlowe SI, Kowalsky PN, Hershey BJ, Levin MJ. Resistance to antiviral drugs of herpes simplex virus isolated from a patient treated with acyclovir. New England Journal of Medicine, 1982; 306(6): 343-6.
134. Ghoke SS, Sood R, Kumar N, Pateriya AK, Bhatia S, Mishra A, Dixit R, Singh VK, Desai DN, Kulkarni DD, Dimri U. Evaluation of antiviral activity of Ocimum sanctum and Acacia arabica leaves extracts against H9N2 virus using embryonated chicken egg model. BMC complementary and alternative medicine, 2018; 18(1): 1-0.
135. Chiang LC, Ng LT, Cheng PW, Chiang W, Lin CC. Antiviral activities of extracts and selected pure constituents of Ocimum basilicum. Clinical and Experimental Pharmacology and Physiology, 2005; 32(10): 811-6.
136. Verma S, Gupta M, Popli H, Aggarwal G. Diabetes mellitus treatment using herbal drugs. International Journal of Phytomedicine, 2018; 10(1): 1-0.
137. Saxena A, Vikram NK. Role of selected Indian plants in management of type 2 diabetes: a review. The Journal of Alternative & Complementary Medicine, 2004; 10(2): 369-78.
138. Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific journal of tropical biomedicine, 2012; 2(4): 320-30.
139. Bilal M, Iqbal MS, Shah SB, Rasheed T, Iqbal H. Diabetic complications and insight into antidiabetic potentialities of ethno-medicinal plants: a review. Recent patents on inflammation & allergy drug discovery, 2018; 12(1): 7-23.
140. Rahman S, Islam R, Kamruzzaman M, Alam K, Jamal AH. Ocimum sanctum L.: A review of phytochemical and pharmacological profile. American Journal of Drug Discovery and Development, 2011; 1: 1-5.
141. Husain I, Chander R, Saxena JK, Mahdi AA, Mahdi F. Antidyslipidemic effect of Ocimum sanctum leaf extract in streptozotocin induced diabetic rats. Indian Journal of Clinical Biochemistry, 2015; 30(1): 72-7.
142. Agrawal P , Rai V, Singh RB; Randomized placebo-controlled, single blind trial of holy basil leaves in patients with noninsulin-dependent diabetes mellitus, Int J Clin Pharmacol Ther, 1996; 34(9): 406-9.
143. Thrimawithana TR, Rupenthal ID, Räsch SS, Lim JC, Morton JD, Bunt CR. Drug delivery to the lens for the management of cataracts. Advanced drug delivery reviews, 2018; 126: 185-94.
144. Kershnar AK, Daniels SR, Imperatore G, Palla SL, Petitti DB, Pettitt DJ, Marcovina S, Dolan LM, Hamman RF, Liese AD, Pihoker C. Lipid abnormalities are prevalent in youth with type 1 and type 2 diabetes: the SEARCH for Diabetes in Youth Study. The Journal of pediatrics, 2006; 149(3): 314-9.
145. Khanna N , Arora D, Halder S, Mehta AK, Garg GR, Sharma SB, Mahajan P.; Comparative effect of Ocimum sanctum, Commiphoramukul, folic acid and ramipril on lipid peroxidation in experimentally-induced hyperlipidemia, Indian J Exp Biol., 2010; 48(3): 299-305.
146. Ali MK, Narayan KV, Tandon N. Diabetes & coronary heart disease: current perspectives. The Indian journal of medical research, 2010; 132(5): 584.