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## Holy basil: Holy herb to multimodal medicine for human health

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### Abstract

The scientific advancement of modern generation to understand the balance between the healthy lifestyle and disease by altering or regulating the expression of genetic activity based on their human genetic makeup. The cause of global humanity is lifestyle related diseases, many of which can be addressed through Ayurveda with its affect on healthy lifestyle and reducing the ill effect of chronic diseases. Ayurgenomics provide a genetic understanding and expression for how phytochemical affects the balance between human health and diseases. There is several evidence of Holy basil phytochemical on clinical and scientific research and confirming their beneficial effects. Tulsi having different medicinal properties like antimicrobial, antiviral, anticancer, antidiabetic, antioxidant, anti-inflammatory and antifertility. The establishment of high correlation of Prikriti and identifying the genomics signature by isolating RNA and DNA studies through "Next Generation Sequencing". Our review based on the advancement of ayurgenomics study directly correlates with the translational and preventive medicinal research.

**Keywords:** holy basil, multimodal medicine, ayurveda

### Introduction

In recent times, focused on aryuveda research has increased all over the world and especially in India. An Ayush has given the huge information of medicinal plants used in various regulatory functional systems in human. The different medicinal plants are source of medicines for number of diseases existing in human race. According to "Rigveda", a medicinal use of plants in Hindu culture is an oldest knowledge information resource. Medicinal plants have an immense therapeutic potential and it is associated with human history for their use in traditional and aryuvedic medicinal system. Plants like Tulsi, Aswagandha, Amla, Brahmi, Gudmar, Satavari, Senna, Neem etc have eminence value as a cure for various human diseases. Their secondary metabolites and their biosynthesized active compounds are important for clinical drugs and many of chemicals <sup>[1]</sup>. Among these, Tulsi have a great potential for human health. It is considered as a "Holy Herb" in India and important symbol of the Hindu religious tradition. Thus it is also known as Holy basil and botanical identification called *Ocimum Sanctum*, belonging to plant family Lamiaceae. Different known and important *Ocimum Sp.* is well characterized in literature <sup>[2]</sup>. Tulsi has been mentioned in the Charaka Samhita, an ancient Ayurvedic text for its Ayurveda with its diverse medicinal properties. It is a rich source of essential oils and aroma compounds. <sup>[3, 4]</sup> *Ocimum sanctum* has immense number of health benefits such as healing power, coughs, fever, common cold, throat infections, respiratory disorders, kidney stones, heart disorders, stress, skin disorder, traditional medicinal practitioners, as expectorants, analgesic, anticancer, antifertility, antiemetic, antiasthmatic, diaphoretic, antidiabetic, antifertility, hypertensive, hepatoprotective, hypolipidmic and antistress agent <sup>[5-7]</sup>. Thus number of Photochemical studies has been carried out to find out the bioactive compound from different medicinal plants including Tulsi which are used for curing of various human diseases and also play an important role in healing but the genomic basis of their medicinal power still need to be explored in detail. With the advent of next-generation sequencing (NGS) technology, thousands of human genomes and expression data sets have been made available across many diseases and normal control individuals; however, their analysis is still incomplete <sup>[8,9]</sup> On the other hand, some genomic and transcriptome study has also been carried on Tulsi plant to understand the mechanism of its medicinal value. Thus now there is a need to pay attention to gene expression and its regulation to understand the human disease process and management <sup>[10]</sup> and simultaneously to know the effect of intake of

medicinal herbs and its genetic basis. Thus cross kingdom genomics is a key to answer the regulation imparted by plant on human metabolic pathways.

**Pharmacological and Medicinal Properties**

**Antibacterial and Antiviral activity**

The wide range of antibacterial and antiviral activity was observed in *O. Sanctum*. The essential oil of *O.Sanctum* was found to possess significant microbial activity against the *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Shigella flexneri* [11]. The studies have shown that cold leaf extract plays vital role against periodontal pathogen in human dental plaque. [12] During the screening activity, the methanolic extracts of *O.Sanctum* have slight inhibition effect on DENV-1 infected viro E6 cells [13]. The replication of herpes and goatpox virus were inhibited in the presence of eugenol compound of *O. sanctum* [14].

**Anticancer Activity**

The *O.Sanctum* leaf extract is a potential source of anticancer agents due to his combinatorial effects of apoptotic, antimigratory and antiproliferative. The ethanolic and essential oil of *O. Sanctum* leaves significantly inhibits the growth of pancreatic cancer cells as well as human fibro sarcoma cells [15]. The essential oil also has ability to inhibit the proliferation of human breast cancer cells by apoptosis and their cytotoxicity effect has shown that it is far better than reseveratrol [16]. The ethanol extract also act as a chemo-preventive and inhibition candidate in lung cancers.

**Antioxidant Activity**

Tulsi have significant ability to scavenge highly active free radicals. The extraction of fresh leaves and stems of *O.Sanctum* yielded many of the antioxidant compounds like cirsilineol, cirsimaritin, isothymusin, isothymonin, apigenin, rosmarinic acid and appreciable quantities of eugenol. Eugenol to be found primary component in *O.Sanctum* and other compound also established good antioxidant activity [17].  
**Anti-inflammatory activity**  
 The appropriate addition of essential oil in the diet may prevent cancer and immune mediated inflammatory diseases. The extracted Eugenol and paracetamol exhibited significant

( $p < 0.05\%$ ) activity when compare with carrageenan control during the anti-inflammatory activity studies on Wistar Rats [18].

**Antidiabetic Activity**

*O. Sanctum* fresh leaves have been widely used in the treatment of diabetes mellitus. The leaves significantly increase the level of superoxide dismutase, reduced glutathione and peroxidised lipid levels appears to be responsible for hypoglycaemic effect [19]. Somasundaram et al explain the combination of glibenclamide and *O. Sanctum* to be more effective in post prandial blood glucose level in type 2 diabetes mellitus [20]. The methanolic extract of *O. Sanctum* shows reduction of blood glucose level in diabetic Wister rats [21]. Aqueous extract of *O.Sanctum* with vitamin E on biochemical parameters and retinopathy in streptozotocin induces the diabetic Albino male rates.

**Antifertility**

The aqueous extracts of the leaves (100 mg/kg) shows the anti-implantation and abortifacient action in rats and identified pseudo pregnancies rate higher in male than the female. The *Ocimum* leaves causes biochemical changes that affects the spermatozoa motility and found that no pregnancies occurred when animal were mated with female mice of proven fertility [22]. Antiulcer The *O. Sanctum* leaf extract significantly prevents chemically induced gastric ulcers [23]. The oil of *O.Sanctum* was administered in the various dose effects in rats and identified that it reduces ulcer index in dose dependent manner [24]. The effect of ethanolic extract of *O.Sanctum* on different offensive factors like free and total acidity, peptic activity and defensive factors like mucin secretion, which play a crucial role in pathogenesis of gastric ulcers in Sprague-Dawley rats [25].

**Key essential Phytochemical and role in Human Health**

Essential oil was extracted from *O.Sanctum* plant parts by three extraction methods 1) Hydrodistillation 2) Steam distillation 3) Solvent extraction [3]. Phytochemical of Tulsi plant contain the Flavonoids, alkanoids, saponins, tannins, anthocynins, and phenols [26-28] Importance of all these phytochemical is list in Table 1:

**Table 1:** *O. Sanctum* phytochemical and its regulation in human body

Name of Compound	Plant Part	Regulated Human Gene	Activity	References
Eugenol	leaf	COX-2, TNF-alpha, PGE2,IL-6, DFF-45,	Antiinflammatory	[29-33]
		MMP9,		
Urosolic Acid	leaf	ERK,CYP1A1,CYP1B1,E 2F1, COX-2	Anticancer	[34-36]
		ERK, p38MAPK, NF-kB	Antiviral	
		STAT-3,CD-31,NF-kb	Anticancer	
Carvacrol	leaf	TNF-alpha, ICAM1	Antiinflammatory	[37-38]
		Dental diseases	Antimicrobial	
Linalool	leaf	SAP1-3, HAC-1	Antifungal	[39-41]
		CD40, IFN, IL-12, p40, IL-13, IL-17F, IL-2, IL-21, IL-23, p19, IL-4, IL-6, TNF-alpha	Anti-tumor	
Caryophyllin e	leaf	HWP1, ALS3,EED1, HGC1, UME6	Antifungal	[42]
		p53,bax,bak1,BCL-2, mdm2,cox-2,cmyb,VEGF,AKT	Anticancer	
Rosmanic acid	leaf	HMGB1	Antiinflammatory	[43, 44]
		CCR3	Anti- Asthmatic	
apigenin	leaf	COX-2, GLUT-1	Anticancer	[45-49]
		hnRNP, GFP	Antiviral	
		NRF2, FOXO1, FOXO3a,NF-kB,p65	Antidiabetic	
Oleanolic acid	Leaf	mTORc, MAPK, NF-kB, iNOS, Cox-2	Anti-tumor	[50, 51]

## Genetic Research

Molecular characterization of Tulsi using RAPD and ISSR markers showed the species specific allelic variation among different varieties [52]. Estimating the diversity of *Ocimum* population was calculated using the genetic distance, bootstrap method and Euclidian distance for improving the plant [53].

Recently genome sequence for Holy basil has been assembled de-novo by, capturing ~410 Mb of genome in total of 9059 super scaffolds and 85,723 protein coding genes. Studies showed that it represents the smallest nuclear genome in family Lamiaceae. It has provided an important resource for identification of important secondary metabolite synthesizing genes, not identified yet from this medicinal and aromatic plant. It will also enhance the understanding of existing knowledge on Tulsi. Further genetic markers can be developed from the genome obtained, which can be used for diversity and marker-assisted breeding. Thus it can help accelerating molecular breeding approach and has opened new horizon for deep genetic study.

Transcriptome of holy basil and sweet basil has also been studied using Illumina sequencing platform and characterize gene related to secondary metabolites and unique essential oil composition in *Ocimum* [54]. A total of 458 genes were identified in *O. tenuiflorum* subtype Krishna Tulsi genome, which are either homologous or directly code for enzymes involved in the synthesis of specialized metabolites [55]. However there is no information on how these gene having significant medicinal properties that cure several human diseases are regulated and their impact in human body.

Thus in spite of having morphology, physiology, genomic and transcriptome information on Tulsi, still non-coding gene information (eg miRNAs) remains unexplored which may give the immense information for human gene regulation.

## Cross Kingdom Genomics

In genome there are three functional class of RNA mainly named as 'Transfer RNA', 'messenger RNA' and 'ribosomal RNA'. [56] The messenger RNA is translated in to proteins with the help of other RNAs like tRNA and rRNA. Other than these categorized RNAs, there are number of different small RNAs which are non-coding RNA molecules (~70 to 300 nucleotides) and thus they are not translated into proteins [57] but play vital role in process of regulation. One of those is microRNAs, encoded by specific genes and functioning through partial base pairing complimentary with target genes in post transcriptional repression of gene [58, 59]. The sRNA or miRNA molecule mobility found within organism helps in the gene silencing among cells and tissues. Gene silencing mainly happen due to sRNA with the same species or different kingdom species. There are many studies existence of cross kingdom gene silencing reported between plant and human, animal cell and parasite etc. Human foods are mainly depends on the plants, It was assumed that researcher would look for the outcome of plant miRNA after food intake and find out the potential effect of plant miRNA on human gene expression.[60] In recent years, small RNA especially miRNA found to be in human circulating system in all parts of our body fluids and regulating the human gene expression. Plant miRNAs cross kingdom analysis with human gene expression gives new evidence of the presence of plant miRNA in human as well as it is potential to act on wide range of human diseases as well as many biological processes [61, 62]. E.g. (a) Moringa and Curcuma miRNA were analyzed and identified

the best possible miRNA and their target roles in human gene regulation [63]. (b) Zhang et al study on rice demonstrate that mir168a binds to exon 4 of LDLRAP1 mRNA and inhibit the level of that protein in liver [64, 65]. (c) miR159 from the different plant source inhibit the cell growth of breast cancer gene(TCF7) and it was tested on the different cell lines. These kind of different studies provide evidence for potentially revolution concept of small RNA cross kingdom analysis between plant and humans`.

Thus in near future, it is very much necessary to study the regulatory role of miRNAs of tulsi on gene expressed in human body to study and understand the mode of mechanism by which tulsi shows curing effect in different human diseases.

## Conclusion and Future directions

Now a day's plants are useful source and it is used in various system of medicine practiced due to their diverse properties. Here we presented the review with experimental detail for small RNA of plant and human cross kingdom gene regulation. The importance of plant Phytochemical constitute with their targeted genes help in cross kingdom evidence of gene regulation. With the help of NGS technology and cross kingdom gene regulation evolve in a future development of human integrative gene silencing networks and novel therapeutic drugs. *Ocimum* ethanobotanical properties and clinical ongoing investigation reported that it is having health promoting qualities.

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