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Ethnopharmacological importance of Salvia hispanica L.: An herbal panacia

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> Abstract---Salvia hispanica L. is commonly known as chia. Chia seeds are currently utilized as a popular superfood because of its nutritional and medicinal value. Chia is a Mexican plant and belonging to Labiatae/Laminaceae family. The scientifically evident higher content of omega-3-alpha linolenic acid is the major reason behind the higher health benefits of Salvia hispanica. The plant also investigated and observed to contain other bioactive proteins, dietary fibers along with antioxidant phytocomponents. It has also been evident that the dietary fiber content of Salvia hispanica is favoring the proper functioning of digestive system, whereas the presence of unsaturated fatty acids exhibits its beneficial effect in controlling the diabetes mellitus. Literature reflects the preventive and curative effect of Salvia hispanica against many diseases like cardiovascular disease, diabetes, obesity, cancer, skin problems, hepatic diseases, gastrointestinal disorders and boosts the immune system. In the last few decades, due to its miraculous therapeutic potentiality Salvia hispanica has raised its market popularity as a potent nutraceutical all over the world. Keeping in view of the therapeutic importance of Salvia hispanica L. The present review is mainly focused on its nutraceutical potentiality.

*Keywords---*Salvia hispanica, Omega-3 fatty acids, proteins, fibers, nutraceutical.

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Introduction

The utilization of natural plants for the diagnosis and treatment of several disorders has been taken into consideration from decades (Pal, 2011; Pal & Gurjar, 2017; Pal & Saha, 2019; Pal et al., 2019; Pal & Mazumder, 2014; Pal et al., 2011). Naturally collected medicament has a vital role in traditional system of medicines. S. hispanica belongs to family Labiateae which consists of 900 species of plants, shrub, and brushes (Valdivia & Tecante, 2015), and most have abundant nutritional and therapeutic values. S. hispanica is receiving an enormous revival because in past it was consumed as staple food by the ancient civilizations of North and Central America. S. hispanica is an annual plant of 1 to 1.5 meter in height. It is a macro-thermal short-day flowering plant, generally in the summers. It is having squared, ribbed and hairy stem. The common name of S. hispanicais originated from the word "chian" which means oil-related materials. Due to the abundant content of Omega-3 S. hispanica is considered as the powerhouse of omega-3. S. hispanica has many other nutrients including proteins, minerals, vitamins, dietary fibers, and other polyphenolic antioxidants which are responsible for major health benefits of S. hispanica (Capitani et al., 2012) and further studies shows that S. hispanica seed has the high amount of linoleic and alpha-linolenic fatty acid (Ullah et al., 2016). For this high nutritional content and therapeutically activities it is also known as functional food and superfood and extensively gaining popularity as potent nutraceuticals. As nutraceutical are mainly the functional foods produce specific pharmacological and therapeutic advantage in addition to nutritional value, mainly these are conventional foods (Trottier et al., 2009; Kalra, 2003). Nutraceuticals are the modified products which are taken from the food sources and are intended to produce more benefits to health, in comparison to traditional product. S. hispanica preparation may assert to inhibit chronic disease, enhance health benefits, setback the aging process, improve the life expectancy and support or protect the structure and function of the human body (Singh & Singh, 2012). Now the impressive fact regarding S. hispanica is the presence of high amount of free fatty acid. S. hispanica oil is extracted, and oil contain maximum 60% of omega-3 (Marcinek & Krejpcio, 2017). However, S. hispanica is not only taken for their nutritional value but also it has the capability to form a mucilage layer when it meets water (Ayerza & Ground, 2005; Cahill, 2003; Ayerza & Coates, 2005; Silva et al., 2016). Moreover, it has been already studied that S. hispanica has the potential against inflammatory disorders, diabetes, cardiovascular diseases, protect the CNS and also have the immune booster property. Therefore, the reason behind of this review article is intended to highlight the overall nutraceutical potential of S. hispanica with scientific evidence.

Chemical constituents

S. hispanica have been used as a functional food and nutritional supplement due to its important bioactive phytocomponents. The principal constituents of the seeds of *S. hispanica* omega-3 alpha-linolenic acid (ALA) which shows the most important effect in the treatment of health problems such as different types of cancer, cardio-associated disorders, and arthritis, etc (Rahman *et al.*, 2017). The leaves of *S. hispanica* were observed to contain several essential oils which have the repellent property, and they cover or protect the plant from the attack of the

insects. The compositions of oils are observed as β -caryophyllene, globulol, tmuroleno, β -pinene, α -humoleno, germacren-B, and widdrol (da Silva *et al.*, 2016). In literature it has been mentioned that S. hispanica contains various active constituents, phenolic acids and free fatty acids. But there are several factors which are responsible in the variation of the concentrations of active ingredient i.e., cultivation place and mode, environmental changes, nutrient quantity, nature, climatic conditions, geographical origin quality of soil and the process of extraction which may also affect the purity of active compounds (Oliveria et al., 2017; da Silva et al., 2016). Moreover, S. Hispanica seeds oil has higher amount of unsaturated fatty acids that is linolenic acid. Furthermore, S. hispanica does not contain any toxic substances and gluten protein, thus ingredients of S. hispanicaseeds are safe and the preparations are also safe and healthy for which its seeds are the major ingredient for the preparation for gluten free diets (Weber et al., 1991). The other chemical constituents are also found in the seeds of S. hispanica such asomega-6, quercetin, caffeic acid, myricetin, kaempferol which are basically flavanols and phenolic compounds (Alcantara et al., 2019).

S. hispanicaseeds has nutritional value because of high content of essential free fatty acid (a- linolenic), which is accomplice with several physiological functions (Chicco *et al.*, 2008). S. hispanica contains high amount of active nutrients as carbohydrates, fibers, lipids, proteins, vitamins, and minerals are in accurate concentrations (Vuksan *et al.*, 2017). The protein content of the S. hispanica varies, and the variation is depending upon the location of the crop and cultivation conditions and is high in S. hispanica seeds than the other grains because it contains nine essentials amino acids (Gazem & Chandrashekarish, 2016). It gives the positive results for the patients who are facing the celiac disease as it is digest easily because S. hispanica is gluten free seed. Protein rich food increase the metabolism of fatty substance which leads to the process of weight loss. It has been already studied that continuous use of protein leads to weight loss and reduce obesity (Pellegrini *et al.*, 2018). After the testing, the most important, and present in high amount, is globulin protein.

On the other hand, the higher dietary fiber in S. hispanica seeds is essential ingredient for the protection of human health against cardio-vascular disease, diabetes mellitus (DM) type 2, and produce anti-carcinoma effect. Its daily consumption had observed to increase the post-meal satiety and subsequently decreases the hunger (Deka & Das, 2017). The dietary fiber in S. hispanica seeds is found to fulfill the daily requirement of fiber to the adult population (Ayerza & Coates, 2004; Kulczynski et al., 2019). Additionally, the nutrient value of the seeds of S. hispanica increases because of the presence of polyunsaturated fatty acids (Jamboonsri et al., 2012; Martinez et al., 2012) which are found as palmic acid, stearic acid, oleic acid and alpha linolenic acid (ALA). ALA is the major fatty acid which is found in the higher quantity approximately 75% (Coates & Yaqoob, 2009). These types of fatty acids are starting precursor for the synthesis of high molecular weight omega-3 polyunsaturated fatty acids ecosapentanoicacid (EPA) and docosahexanoic acid (DPA). These fatty acids are not synthesized by human body, so these fatty acids are also known as essential fatty acids (Calder & Yaqoob, 2009; Domingo, 2007). Vitamins are play a vital role in repairing the physiological system such as regulate the hormonal secretion according to the body demand cell division and tissue differentiation (Suri *et al.*, 2016). *S. hispanica*seeds has most prominent vitamin is vitamin B and niacin which add on its nutritional value (Bushway, 1981) and efficacy against oxidative stress. Apart from these, *S. hispanica* contains various minerals which are potassium, calcium, phosphorous and the concentration of these minerals is very high than the 100g of milk, and have some traces of minerals magnesium, iron, zinc, copper (Carrillo *et al.*, 2108). In the seeds of *S. hispanica*phenolic contain high level of chlorogenic acid, rosmerinic acid, caffeic acid, querencetin cinnamic, gallic acid, kaempferol, myricetin. Furthermore, it also has traces of isoflavones such as diadzein, glycitein and genistein. rosmarinic acid and diadzein are the main components of *S. hispanica*seed together with caffeic acid, mycertin, quercetin etc (Rahman *et al.*, 2017). Table 1 and Figure 1 elaborate the findings on chemical components investigated by different coworkers.



Figure 1. Active composition of S. hispanica seeds

S.No	Chemical	Therapeutic actions
	constituents	
1.	Omega-3 alpha linolenic acid <i>w</i> -3 alpha-linolenic acid (ALA)	 An essential fatty acid (Heuer <i>et al.</i>, 2002) Decrease triglycerides and cholesterol level, results lower hypertension and heart related diseases (Jeong <i>et al.</i>, 2010) Anti-inflammatory action (Simopolus, 2002) Cardio-protective and hepatoprotective activity (Poudyl <i>et al.</i>, 2010) Anti-diabetic action
		• Lower the risk of autoimmune disorders cancer (Ali <i>et al.</i> , 2012)
2.	Omega-6 linoleic acid	 Anti-inflammatory effect Antihypertensive (Betti <i>et al.</i>, 2009) Antithrombotic activity (Dubois <i>et al.</i>, 2007) It works inversely to the alpha-linolenic acid; thus, the resultant balancedstatus supports the good health.
3	Dietary fibers soluble and insoluble	 High fiber content enhances satiety, decrease energy intake (Vuksan <i>et al.</i>, 2007) Promote weight loss Maintain frequent peristaltic movement of intestine Reduce intestinal tract disorder (Vazquez- Qvando <i>et al.</i>, 2010)
4.	Myricetin, Kaempferol, Quercetin, Caffeic acid (Flavanols and Phenolic acid)	 Antioxidant activity (Taga <i>et al.</i>, 1984) Anti-inflammatory activity (Iglesias-Puig & Haros, 2013) Anticancer activity (Ali <i>et al.</i>, 2012)

Table 1: Active components found in Salvia hispanica with their identified activity.

Pharmacological Actions

The consumption of *S. hispanica* extracted with water is famous in runners for its nutritional value to run many miles (Lopez *et al.*, 2018; Scapin *et al.*, 2016). Apart from this, *S. hispanica* shows good potentiality against inflammation and reduces blood glucose level as anti-diabetic agent, in the treatment of dyslipidemia and also provides the protection to the visceral organs (Iglesias & Haros, 2013; Nieman *et al.*, 2009). In general, the internalization of *S. hispanica* in foods enhance their physicochemical and nutritional characteristics. *S. hispanica* seeds is used in bakery, to enhance the concentration of proteins, unsaturated fatty acids, antioxidants and dietary fiber of bakery products (Timilsena *et al.*, 2016) (Figure 2).

Antioxidants

The seeds of S. hispanica are the therapeutically active because of their chemical constituents, on studying the seeds of S. hispanica result that it has some chemical constituents which has the antioxidant property, and the constituents are tocopherols, caffeic acid, chlorogenic acid followed by quercetin, kaempferol (Taga et al., 1984; Ayerza & Coates, 2001). These compounds show synergistic antioxidants and potentiate the antioxidant activity of S. hispanica seed (Ayerza & Coates; Ixtaina et al., 2011; Fernandez et al., 2006). Quantity of tocopherols in S. hispanica seeds was found to be approximately like peanut oil, but flaxseed contain more tocopherols than S. hispanica and other cereals also have higher antioxidants than the S. hispanica, like sunflower and soybean (Tuberoso et al., 2007). Chlorogenic and caffeic acid save the human body against the reactions of free radicals. Not only these antioxidants inhibit the process of oxidation of fatty acids and quercetin but also have the good antioxidant property with cardioprotective effect (Pandey & Rizvi, 2009). All these antioxidants those are found in S. hispanica have potent antioxidant property than ferulic acid, Ascorbic acid and vitamin E (Taga et al., 1984; Ayerza & Coates, 2001; Reyes-Caudillo et al., 2008)



Figure 2: Available neutraceuticals of S. hispanica preparations

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Cardio-protective effect

Eicosapentaenoic acid and α -linolenic acid content of *S. hispanica* seeds are observed to show important function in the synthesis of several important biochemical compounds such as leukotrienes, thromboxanes and prostaglandins which perform various physiological functions (Romankiewicz *et al.*, 2017).On the other hand, high content of omega-3 fatty acids in the seeds of *S. hispanica* has the capacity to inhibit the calcium channel and sodium channel dysfunction which otherwise results to hypertension. Omega-3 fatty acid also enhances the cholinergic tone heart rate variability and protects from ventricular tachycardia (Leaf & Kang). Omega-3 fatty acid is a group of 3 essential fatty acids like eicosapentaenoic acid, α -linolenic acid and docosahexanoic acid, while omega-6 fatty acids are composed of arachidonic acid and linoleic acid contributing the maintenance of normal functioning of myocardium (Pawlosky *et al.*, 2003).

Skin curative agent

After the extraction of *S. hispanica* oil an experimental study was conducted to observe the dermatological effect of omega-3 fatty acid by its topical application. Its topical preparation is prepared which contain 4% of oil and applied for 8 weeks. After the application, the area of skin is examined and observed that improved skin moisture, cure lichenification and treat prurigo nodular is in all skin patients (Jeong *et al.*, 2010).

ACE (Angiotensin Converting Enzyme) inhibitory effect (Antihypertensive activity)

To target the most prevalent disorder of present-day hypertension, one scientific investigation was carried out to extract and isolate the peptide contents of the seeds of *S. hispanica*, and then the testing for the ACE-I inhibitory activity in terms of purified fraction and hydrolysate was performed. After the completion of the test timing the inhibitory action was examined, that results hydrolysate showed approximately 60% inhibition, while purified fraction produced approximately 70% inhibition. Amino acid content is also estimated and studied and found that some amino acid also plays the role of the inhibitory action of ACE-I and suggested as the isolated natural bioactive peptide have inhibitory action of ACE-I. Additionally, it was also supported for its use as an antihypertensive agent (Segura-Campos *et al.*, 2013).

Immunomodulator

In an investigation the seeds of *S.hispanica* were studied for testing its activity of on immune system. It was started with 23 days old male wistar albino rats, and the indicator for immunity was taken as the level of thymus and serum IgE. The study revealed that *S. hispanica* administered animals were free from any difference in the body weight, whereas IgE level was considerably increased in comparison with control which concluded its immunostimulatory potentiality (Fernandez *et al.*, 2008). 5956

Hypoglycemic effect of S. hispanica

The action of *S. hispanica* protein on glucose content, lipid profile, functioning of liver and gut of the animal was performed, that results revealed that the test compound treated animals have low glucose level, decrease triacyl glycerides level and also reduce the concentration of LDL, VLDL, HDL means *S. hispanica* seed have hypoglycemic activity (Silva *et al.*, 2016; Saha *et al.*, 2016; Enes *et al.*, 2020). While weight is lower than control group and intestine wall become thickened. Therefore, declaration of the study continuously used *S. hispanica* seeds which has good digestibility, and better lipid profile and work as a hepatoprotective agent and enhance the functioning of liver and intestine (Figure 3).



Figure 3: By the previous study which are conducted to examine the effect of *S. hispanica* on human glucose level suggest that the glucose balance in the blood serum is maintained by the AKT activation, gluconeogenesis and glycolysis pathways. *S. hispanica* oil enhanced the expression of insulin receptor, which contributing to insulin binds to receptor and signaling to phosphorylate AKT. Phosphorylated AKT inhibits FOX01 to move to nucleus and to begin transcription of gluconeogenesis enzymes, regulating glucose synthase. *S. Hispanic a*hydrolyzed phenolic compounds which participates to decrease glucogenic pathway.

Anticancer activity

As a rich source of omega-3, omega-6and polyunsaturated fatty acids (PUFAs), the anticarcinogenic activity of *S. hispanica* seeds were targeted against prostate cancer cells which was performed by the MTT test⁷². The prostate cells were placed into the medium and taken in a microtiter plate (96 well) and further, Incubated microtiter plate in Co2 incubator for72 hours. The cells were treated with other concentration preparations of *S. hispanica* in 0.1% DMSO was added for 48 hours at the same incubation conditions. On checking the microtiter plate for the viability of cells it was confirmed that *S. hispanica* can also be used in the management of prostate cancer as reduced the cell viable count.

Antimicrobial activity

Extract of methanol, ethyl acetate and hexane extracts of the seeds of *S. hispanica* were tested against bacteria. Extracted product shows the inhibitory action against pathogenic bacteria. Furthermore, highest zone of inhibition was seen with methanolic extract. In that investigation it was that the aqueous and methanolic extract of *S. hispanica* shows good antibacterial activity against the disease-causing bacteria (Divyapriya *et al.*, 2016). The microbial inhibitory action of *S. hispanica* may be due to the presence of antioxidants and fatty acids (Ayerza & Coates, 2000).

Anti-inflammatory activity

Considering rheumatoid arthritis (RA) is associated with pain in joints, redness, swelling in and stiffness resisting joints' movement, *S. hispanica* seeds mucilage and oil were investigated for the treatment of arthritis. Freeze-dried mucilage and *S. hispanica* oil was tested against inflammation by using Spargue-dawley rats. Inflammation was induced in selected obese or non-obese rats by the application of inducing agent (Freund complete adjuvants). After the study a well-defined and clear conclusion was fixed that *S. hispanica* has significant anti- inflammatory action in adjuvant-induced arthritic rats (Chawla *et al.*, 2021).

Considering *S. hispanica* is an important and rich source of proteins, it showed inhibitory activity for trypsin. Additionally, its antitryptic activity is also due to the presence of other above mentioned nutritional composition and phenolic content (Souza *et al.*, 2017).

Anticholesterolemic action

High concentration of blood HDL-cholesterol level is the direct sign of development of cardiovascular disease in humans (Rasheed & Cummins, 2018). Due to high concentration of dietary fiber and unsaturated omega-3 fatty acids content of the seeds of *S. hispanica* reduce the level of serum cholesterol in humans. Recently, it has been found that the proteins and peptides of *S. hispanica* can inhibit the key markers of cholesterol synthesis, HMG- CoA reductase (de Saliva *et al.*, 2017; Coelho *et al.*, 2018).

Conclusion

The extensive review on S. hispanica unfolded many important medicinal benefits of this plant with their scientific benefits. This article also highlighted the relevant presence of proteins, fibers, lipids and other active constituents in S. hispanica seeds which were again found to scientifically identified. The major peptide sequences have observed to possess very important biological potentials mainly hepato-protective, skin curative, high nutritional value and hypoglycemic properties. Along with these other bioactive peptides also possess the biological activity. These activities are mainly investigated to be possessed by the presence omega-3 alpha linolenic acid. The seeds of S. hispanica also composed of high number of polyphenols includes myricetin, caffeic acid and others which possess antioxidant property. As the major bioactive phytocomponents of Chia seeds likefibers, proteins, a-linolenic acid and omega fatty acid are having many other beneficial effects of normal physiology of human systems, these can also be explored for many other untouched pharmacological activities for the betterment of mankind. The observed nutraceuticals are having pharmaceutical and nutritional benefits with their growing popularity and increased consumption. The chia seeds are less explored for their overall psych protective and gastroprotective effects which are the major areas to be scientifically proven with responsible mechanism of action for the development of full proof nutraceutical. Additionally, except its mucilage some more advanced and targeted formulations can be developed for its better therapeutic application. However, more studies are necessary for the clarification of molecular structure and pharmacological actions. This comprehensive review will be helpful for further explore of important nutraceuticals of different parts and mainly S. hispanica for the management of different diseases with better mechanism-oriented investigations.

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