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INTRODUCTION AND IMPORTANCE OF MEDICINAL PLANTS RELATED TO HUMAN HEALTH CARE AGAINST SWINE INFLUENZA VIRUS

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Abstract:

As per the literature, medicinal plants are used in the prevention and treatment of various chronic diseases including Swine flu. The therapeutic properties of various medicinal plant products are reported and also showed structure activity relationship of some important and potentially useful plant based formulations for preclinical or clinical evaluation. In-depth information of these medicinal plant products which provides lot of information about some active components and used in the form of antioxidants, antidiabetic, antihypertensive, analgesic, anticancer, antidepressant, antiasthma, antimicrobial, anti-inflammatory agents and also used as immunomodulators. In view of this, we focused on one of these diseases especially Swine flu that are highly prevalent in India. In 2015-2016, lot of swine flu cases were reported and few of them were survived after treatment. Recently, researchers start focusing on various medicinal plant products in order to reduce the burden of infectious disease i.e. swine flu. In the present study, we mentioned about some medicinal plants that are required for eliminating swine flu disease.

Key words: *Medicinal plants; swine flu; infectious disease*

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INTRODUCTION:

As per the literature, number of medicinal plant products are already identified and studied as well as claimed its various immunobiological properties. These properties could be due to the presence of various chemical compounds in the form of primary and secondary metabolites for various biological functions [1, 2]. For the last twenty years, number of bioactive compounds in the form of flavonoids, terpenoids, alkaloids, glycosides etc. have been identified by various researchers [2-6]. These metabolites are more beneficial related to human health and working on the same way as pharmaceutical drugs but the major difference is to showed less adverse effects in case of medicinal plant products. Recently, researchers worked on various medicinal plant products and isolated various active compounds that are useful for animal including human [3-6]. The most important drugs i.e. aspirin, digoxin, quinine, and opium etc. isolated from medicinal plant products as mentioned in the literature [7, 8]. One of the most familiar example i.e. Quinine isolated from the bark of Cinchona tree and is used for the treatment of various diseases especially Malaria, arthritis and Babesiosis [9]. In contrast, one of the active ingredients are identified and isolated from medicinal plant products and determining through HPTLC, HPLC, NMR and C13 analysis. Number of phytochemicals already exists within the medicinal plant and may be transformed to make new pharmaceutical drug i.e. if flavonoids/terpenoids/glycosides isolated from medicinal plant products i.e. leaves/stem/roots and actually it is present as well as isolated in crude form [2-6]. Lot of biochemical compounds are present or exists within that crude form and it is identified through HPLC. These activities of these secondary metabolites are not because of crude form, only it will happens when any active constituent is present in a large quantity.

In general, secondary metabolites are used in the form of toxins (predation) and also used as pheromones (attract insects for pollination). So, these metabolites also showed some therapeutic actions in humans and is able to produce various types of drugs e.g. inulin from the roots of dahlias, codeine from poppy; digoxin from foxglove etc. [7-8] In short, these medicinal plants have some ability to synthesize various secondary metabolites with some bioactivities. Number of bioactive compounds isolated from secondary metabolites that played an important role in microbial pathogens, competing with other plants and faciliting pollination and reproduction. All these compounds are generally biosynthesized through series of enzyme catalyzed reactions using simple building blocks in different ways. There are several main biosynthetic pathways in plants, including shikimic acid pathway (phenylpropanoids), mavalonic acid pathway (quinones), 2-C-methyl-D-erythritol-4-phosphate pathway (quinones), amino acid pathway (alkaloids), acetate-malonate pathway (fatty acid, phenols and quinones) and combined pathways (flavonoids) [10]. Globally, thousands of plant derived medicines used in the form of traditional medicine for the treatment of various intracellular and extracellular infections. So, majority of these medicinal plants are used alone or in combination with other specific protein antigens. Majority of them have not been scientifically investigated, there is little scientific or clinical data supporting their therapeutic use.

According to the literature, one third of the world population is totally relied on medicinal plant products for human health care e.g. US (> 25%), china and India (>80%) etc. These countries provide two third of the medicinal plants that should be used in modern system of medicine. In Asian countries, people especially villagers generally use medicinal plant products for healing, and these plants are collected either in the surroundings of the villages. Unfortunately, most of these medicinal plants that are clearly affected by biodiversity loss, environmental degradation and a lack of sustainable harvesting practices [11]. Overall, these impacts are also exacerbated by climate change, and high levels of poverty. In contrast, rapid deforestation are one of the real threats that often affect medicinal plant habitat in all over the world and may affect people's knowledge related to the use of medicinal plants. Furthermore, knowledge on these medicinal plants is still hardly documented at all [11, 12].

One of the most interesting studies i.e. antimicrobial studies and these studies are included as one of the hot topic related to medicinal plant products. Lot of research work is still going on and reported some medicinal plants that are responsible for reducing the burden of various infectious diseases. Some of the medicinal plants [13-17] are *Butea frondosa, Syzygium cumini, Calotropis gigantea, Emblica officinalis, Terminalia arjuna* etc. The control of these microbial infections is increasingly complicated but majority of them is still resist against some available drugs that are available. In an effort to search for new antimicrobial agents that are needed to reduce the burden rate of infectious agents. In this regard, various studies were conducted against microbial pathogens with respect to medicinal plant products in order to isolate and purified secondary metabolites and its derivatives.

As per Ayurveda and Unani, these medicinal plants are included as one of the major systems of indigenous medicines. One of these diseases, Swine flu (Swine influenza or pig influenza or pig flu) is included under the category of respiratory system disorder and is generally caused by H1N1 virus [18]. In 2009, swine flu strains include influenza C and subtypes of influenza A (H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3). Firstly, swine flu case was observed in humans in Mexico, 2009. Six of these genes are totally similar to the H1N2 influenza virus that was found in pigs. Generally, the transmission of swine flu virus from pigs to humans is not always common and does not always lead to human flu, often resulting only in the production of antibodies in the blood. If transmission does cause human flu, it is called zoonotic swine flu. The most common symptoms (chills, headache, muscle pains, weakness etc.) that are observable in humans with respect to zoonotic swine flu that is totally similar to those of influenza illness [19, 20]. In 2010, World Health Organization declared swine flu as pandemic disease officially over. In India, number of cases up to March 2015 related to swine flu (around 31,156 positive test cases and 1,841 deaths) are reported.

Swine influenza virus

Swine influenza virus, strain of the influenza family of viruses that is highly endemic in pigs. This virus is reported as an emerging viral infection and represents one of them major global public health problem (**Fig.1**.). Thousands of cases related to swine flu that are reported in the year 2016. This new infection can be seen around the world in the present day [21, 22]. Recently, one of these endemic diseases i.e. Influenza (family *Orthomyxoviridae*) showed several subtypes i.e. type A, B and C that are reported. Out of these, Influenza type A is highly antigenic as compared to other subtypes and responsible for causing epidemic influenza whereas influenza B subtype showed less variation and causes less frequent epidemic and subtype C is antigenically stable and causes only mild infection [21, 22].

Influenza viruses (single-stranded, RNA genome**)** that encodes all the viral proteins and it is divided into eight segments. All these segments are coated with nucleoprotein (NP) in order to protect the fragile RNA. Afterwards, RNA is replicated through polymerase enzyme which is composed of three different proteins i.e. PB1, PB2, PA. Overall, combination of RNA, nucleoprotein and polymerase are collectively called as ribonucleoprotein particle (RNP). In addition, two other viral proteins are reported i.e.NS1 (non-structural protein 1; prevent the cell from detecting the virus and shutting down important cellular pathways) and NS2 (non-structural protein 2; assembly of new viruses), are also present within the virus in small amounts [21, 22].

Influenza (virion; roughly spherical; enveloped virus), two major types of proteins are reported i.e. hemagglutinin (virus bind to cells in the respiratory tract by binding to sialic acid on the cell surface) and neuraminidase (newly made viruses release from infected cells by cutting up sialic acids so they fall off the cell). In contrast, matrix protein 2 (M2) is the other type of protein that are found in the viral membrane. It is an ion channel, which means it lets the pH inside the virus change as the pH outside the virus is changed. The inside of the viral membrane is coated with M1 (matrix protein 1).These are the proteins (hemagglutinin, H and neuraminidase, N) that determine the subtype of influenza virus (e.g. H1N1, H2N1 etc.). Both these proteins especially neuraminidase, target for antiviral drugs e.g. Relenza and Tamiflu that are required for immune response in order to protect against microbial infection [23, 24].

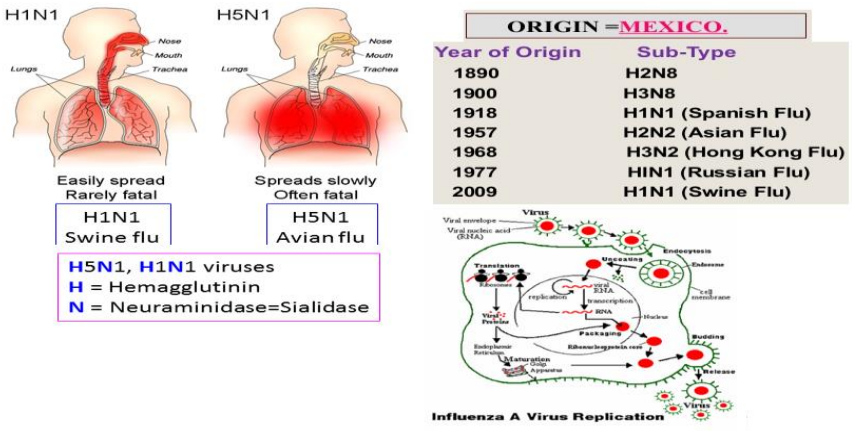

Fig.1: Swine flu. Mentioning about its origin and also described its life cycle of influenza A virus replication.

Lot of cases related to Swine flu disease are reported in India (2016-2017). One of the most familiar example is observed in Pune where kids (< 10 years) and adults (31-50 years) under this age group emerged as one of the most sufferer related to swine flu infection, latest report revealed by Pune Municipal Corporation. In 2016, more than 160 cases were positive for swine flu disease and nearly about 25 patients are critically ill and have been put on ventilator. Normally, children under or below the age group of 5 years are not exposed to H1NI or any other type of influenza virus but children in the age group of 5-10 years, there is direct contact with other kids and chances of infection rate are more and easy to transmit the infection. In addition, swine flu infection rate in adults are more because of cardiovascular infections especially diabetes, hypertension and obesity as compared to children. In this regard, researchers focused on medicinal plant products in order to isolate the metabolites and determined anti-swine flu titre or examined antibody production against these swine flu protein antigens. In this study, we prepared a list of plants that are responsible and showed its protective response against these protein antigens related to swine flu as shown in **Table 1.**

Table 1: List of medicinal plants that are useful for swine flu treatment

S.NO.	Plant name	Family	Effective part and its constituents	Biological properties
1	*Zingiber officinale* [25]	*Zingiberaceae*	Roots; zingerone, shogaols, and gingerols; volatile oils (gingerol) with sulphur-containing compounds (allicin, alliin, and ajoene), and enzymes (allinase, peroxidase and myrosinase)	TNF-α, anti-influenza cytokine, is reported in ginger and is known to fight cold, fever and flu conditions, and also worked as anti-inflammatory agent.
2	*Alium sativum* [26]	*Alliaceae*	Oil-soluble compounds i.e. sulfides (Diallyl sulfide, diallyl disulfide, diallyl trisulfide and allyl methyl trisulfide, dithiins, and ajoene); Water-soluble compounds i.e. cysteine derivatives (S-allyl cysteine, S-allyl mercaptocysteine, S-methyl cysteine and gamma-glutamyl cysteine derivatives).	Antiviral effect against para influenza virus type 3 and human Rhinovirus type 2.
3	*Aloe vera* [27]	*Asphodelaceae*	Leaves; main constituents are amino acids, anthraquinones, enzymes, minerals, vitamins, lignins, monosaccharide, polysaccharides, salicylic acid, saponins, and sterols	Useful plant, getting relief from swine flu. Mixed in equal proportion i.e. Aloe Vera juice and vitamin C intake used as powerful way to prevent such type of diseases especially swine flu.
4	*Withania somnifera* [28]	*Solanaceae*	Anaferine, anahygrine, beta-sisterol, chlorogenic acid, cysteine, cuscohygrine, pseudotropine, Scopoletin, somniferinine, withaferin α, withanine, withananine and withanolides.	Withaferin A showed potential to attenuate the neuraminidase protein of H1N1 influenza.
5	*Curcuma longa* [29]	*Zingiberaceae*	Diarylheptanoid compounds are reported i.e. curcumin	Hepatoprotective, cardioprotective,

			(curcumin I); demethoxycurcumin (curcumin II); 1-(4-hydroxy-3-methoxyphenyl)-7-(3, 4-dihydroxyphenyl)-1, 6-heptadiene-3, 5-dione; tetrahydroxycurcumin; 1,5-epoxy-3-carbonyl-1,7-bis(4-hydroxyphenyl)-4,6-heptadiene; 1,7-bis-(4-hydroxyphenyl)-1,4,6-heptatrien-3-one; 4"-(4"'-hydroxyphenyl-3-methoxy)-2"-oxo-3"-butenyl-3-(4'-hydroxyphenyl)-propenoate etc.	hypoglycemic, anti-amyloidogenic, antifungal, parasiticidal, antioxidant, chemo-resistance, radio-resistance activities etc.
6	*Azadirachta indica* [30]	*Meliaceae*	Neem oil (nimbin, nimbinin and nimbidin); β-sitosterol; Azadirachtin	Of the 3 neem compounds—hyperoside, nimbaflavone and rutin—hyperoside are effective against swine flu.
7	*Aegle marmelos* [3]	*Rutaceae*	Leaves (skimianinc, sterol and aegelin)	Medicated oil prepared from bael leaves gives relief from recurrent colds and respiratory infections.
8	*Litchi chinensis* [31]	*Sapindaceae*	Fruit polyphenols	Oligonol, low molecular weight polyphenol obtained from lychee fruit extract inhibits proliferation of influenza virus by blocking reactive oxygen species-dependent ERK.
9	*Echinacea purpurea* [32]	*Asteraceae*	Polysaccharides, caffeic acid derivatives (including cichoric acid), alkylamides, and glycoproteins.	Fresh alcohol plant extract can block the replication of relevant respiratory tract pathogens in-vitro (Hong Kong flu, seasonal influenza), H5N1 (e.g. bird flu, human pathogen), H7N7 (e.g. avian influenza, also human pathogen), H1N1 (human influenza) and H1N1 (Mexico influenza, swine flu, current pandemic).
10	*Camellia sinensis* [33]	*Theaceae*	Rich in polyphenolic compounds and catechins.	Derivatives of catechin exerted inhibitory effects for all six influenza subtypes tested including three major types of currently circulating human influenza viruses (A/H1N1, A/H3N2, and B type), H2N2 and H9N2 avian influenza virus.

In 2015-2017, Swine flu has been declared as a pandemic disease by the World Health Organization. Thousands of swine flu cases were reported in the past and most of these people were suffered through direct contact with pigs. Out of these swine flu strains especially HIN1 virus contained some genetic material of swine, bird and human influenza virus. This disease showed lot of symptoms that are reported in both adults and children. In this regard, swine flu natural remedies or treated with some herbal remedies that considers some better treatment options and showed less toxic effect. So, these medicinal plants or plant based molecules or candidates tried to use as medicines against this disease and most importantly, it showed less side effects as well as compared to synthetic based drugs. Numerous medicinal plants were reported and showed better activity against many types of diseases, intracellularly or extracellularly. In addition, these medicinal plants also showed some antibiotic properties as well.

In short, Ayurveda promotes the concept of immunity against various infectious diseases. If our immune system is strong none of the pathogen will effects our health. In addition, Ayurvedic comprised of complex molecules in the form of primary and secondary metabolites that are highly effective in preventing swine flu infection rate. Moreover, these medicinal plants are used to relieve swine flu symptoms, and boost the immune system against H1N1 virus.

CONCLUSION:

In view of the challenges, disputes and problems posed by swine flu that are more prevalent in some countries. In an effort to provide some prophylactic or therapeutic option in order to reduce the burden of swine flu disease. In this study, we showed some medicinal plants with well known, multiple spectrum of immunobiological effect and also showed direct antiviral effect against swine flu and other influenza viruses is surprising. Few of them, antiviral drugs are already available in the market for treating swine flu disease but due to its side effects, scientists are now, turn their attention towards medicinal plant products and tried to isolated molecules in crude form or pure molecules for eliminating this disease in all over the world.

AUTHORS CONTRIBUTION:

This work was carried out in collaboration between two authors. Dr. Amit Gupta designed the field study whereas Shubham Gaikwad gathered some information about medicinal plants and swine flu related to his M.Sc. Biotechnology dissertation work under Dr. Amit Gupta guidance.

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