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## A Review of H3N2 Virus Diagnosis, Treatments and Prevention and Importance of Indian Medicinal plants against Influenza.

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### ABSTRACT

In the present review, an attempt has been made to gather the information about Influenza virus, specifically H3N2 virus. Influenza a H3N2 is a seasonal virus and the occurrence of influenza infections normally peaks during season changes. In this paper an attempt also been taken to collect the anti- influenza drugs with special reference to a list of medicinal herbs. The influenza virus causes a highly infectious, acute febrile respiratory illness that is extremely contagious. In humans, it is caused by influenza A (genus influenza virus A) and influenza B (genus influenza virus B) Drug-resistant variants of human and avian influenza viruses are becoming more common, the greatest novel synthetic medicines are neuraminidase agents' oseltamivir and zanamivir. Though there are several ways to reducing the negative effects of influenza and its subsequent problems, herbal medicines are favored due to their less adverse effects and inexpensive cost. A list of medicinal herbs with anti-influenza and other therapeutic properties and herbal medicines used to treat colds and influenza has been prepared. This study highlights anti-influenza compounds and other therapeutic properties and herbal medicines used to treat colds and influenza in rural areas of India. This review will definitely help for the researchers as well as clinicians to develop drugs or compounds against the virus, further it may be used to conduct experimental and clinical trials to study the underlying mechanisms and efficacy of antiviral properties of Indian medicinal plants.

**Keywords:** influenza, herbal medicines, therapeutic properties, clinical trials, Indian medicinal plant

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## INTRODUCTION

Viruses are a serious threat to the health of people in all parts of the world. For most bacterial diseases, several effective drugs are available, however, viral diseases are often difficult to treat primarily because viruses spread and mutate very rapidly. The control and treatment of a viral infection depends mainly on the availability of antiviral drugs, which are few and usually are not virucidal but simply prevent replication in the host. It has become imperative to develop effective medical strategies for the management of common viral diseases like influenza, which can assume pandemic proportions and become a major threat to humanity. <sup>1</sup> Influenza is a virus that is widely found in the world. Influenza virus is an RNA virus that often causes many deaths due to its very fast mutation rate. Variant influenza viruses are swine-origin influenza A viruses that are rare causes of influenza virus infection in humans. From January 2005 through June 2011, only 35 US cases of variant influenza virus infection were reported to the Centers for Disease Control and Prevention (CDC). H3N2 influenza A virus: "Seasonal Flu being a contagious disease can spread from person to person through droplets from an affected person's cough or sneeze or through contact of droplets on hands and surfaces. This self-limiting infection lasts for about 5-7 days with minimal morbidity and mortality," The H3N2 subtype of influenza A is currently the main cause of respiratory illness, the other symptoms of flu are often accompanied by low-grade fever at the beginning of the symptoms, muscle aches, and body weakness (fatigue) . Plants have always been the primary choice for preventing and treating various diseases faced by human beings, and contain specific or broad-spectrum active compounds for almost any type of disease .<sup>2</sup> People living in rural areas still have an especially rich medicinal plant repertoire. Although herbal cures such as rosehip tea, peppermint-lemon tea and garlic-lemon tea, which are used to prevent and treat flu outbreaks, are well known by the local people, the vast majority of them and their anti-influenza effects have not yet been studied natural ingredients in recent times. <sup>2</sup> Therefore, natural products such as traditional herbs show great promise in the development of potentially effective new antiviral drugs. Particularly, recent studies on phytochemicals, such as quercetin, chlorogenic acid, mentofin, and linalool abundantly found in many plants and vegetables, eliminate the efforts and huge costs of finding lots of antiviral vaccines that need to be renewed every year and allow us to be more optimistic about the successful management of the next influenza outbreaks.

On August 3, 2016, the Ohio Department of Health Laboratory reported to Centre for Disease Control and prevention that a respiratory specimen collected on July 28 from a male aged 13 years who attended an agricultural fair in Ohio during July 22–29, 2016, and subsequently developed a respiratory illness, tested positive by real-time reverse transcription–polymerase chain reaction

(rRT-PCR) for influenza A(H3N2) variant\* (H3N2v). The respiratory specimen was collected as part of routine influenza surveillance activities. The next day, CDC was notified of a child aged 9 years who was a swine exhibitor at an agricultural fair in Michigan who became ill on July 29, 2016, and tested positive for H3N2v virus at the Michigan Department of Health and Human Services Laboratory. Investigations by Michigan and Ohio health authorities identified 18 human infections linked to swine exhibits at agricultural fairs. To minimize transmission of influenza viruses from infected swine to visitors, agricultural fair organizers should consider prevention measures such as shortening the time swine are on the fairgrounds, isolating ill swine, maintaining a veterinarian on call, providing hand washing stations, and prohibiting food and beverages in animal barns.

## DESCRIPTION

Influenza-A H3N2 variant viruses (also known as “H3N2v” viruses) with the matrix (M) gene from the 2009. The majority of A(H3N2) virus infections resulted in clinically mild, uncomplicated upper respiratory tract disease. Predominant findings among uncomplicated pandemic cases included malaise, fever, myalgia, cough, headache, coryza, and sore throat.<sup>3</sup> H1N1 pandemic virus were first detected in people in July 2011. The viruses were first identified in U.S. pigs in 2010. During 2011, 12 human infections with H3N2v were detected. During 2012, there were multiple outbreaks of H3N2v resulting in 309 reported cases.

## History

The 1968 pandemic was caused by an influenza A (H3N2) virus comprised of two genes from an avian influenza A virus, including a new H3 hemagglutinin, but also contained the N2 neuraminidase from the 1957 H2N2 virus. It was first noted in the United States in September 1968.

## Etiology

Influenza viruses belong to the family of viruses termed “*Orthomyxoviridae*”, an RNA type virus with diverse antigenic characteristics.<sup>4</sup> H3N2 virus contained two genes derived from a low-pathogenicity avian influenza A virus and six genes from the A(H2N2) virus that had been circulating among people since its emergence to cause the 1957 H2N2 pandemic.

## Epidemiologic Investigation

Novel influenza viruses are different from currently circulating human influenza H1 and H3 viruses and have the potential to cause a pandemic if the virus is efficiently transmitted from person to person. In the United States, human infection with a novel influenza A virus is nationally notifiable, and globally, it is a reportable event under International Health Regulations 2005. The

influenza virus has caused recurrent epidemics of acute febrile syndrome every 1 to 4 years for at least the recent centuries. The first epidemic report of an influenza-like illness was noted in 1173–74,3 but the first definitive epidemic was reported in 1694. The greatest pandemic in recorded history occurred between 1918 and 1919, when approximately 21 million deaths were recorded worldwide. It was among the deadliest events in reported human history. Afterward, 3 other pandemics occurred in the 20th century: the 1957 H2N2 pandemic, the 1968 H3N2 pandemic, and the 2009 influenza A (H1N1) virus (pH1N1) pandemic.

In 1997, human infections with the HPAI A(H5N1) virus were reported during an outbreak in poultry in Hong Kong SAR, China. Since 2003, this avian virus has spread from Asia to Europe and Africa, and has become endemic in poultry populations in some countries. Outbreaks have resulted in millions of poultry infections, several hundred human cases, and many human deaths. The outbreaks in poultry have seriously impacted livelihoods, the economy and international trade in affected countries. Other avian influenza A(H5) subtype viruses have also resulted in both outbreaks in poultry and human infections.

In 2013, human infections with A(H7N9) virus were reported for the first time in China. Since then, the virus has spread in the poultry population across the country and resulted in over 1500 reported human cases and many human deaths.

Other avian influenza viruses have resulted in sporadic human infections including the A(H7N7) and A(H9N2) viruses. Some countries have also reported sporadic human infections with swine influenza viruses, particularly the A(H1) and A(H3) subtypes.<sup>5</sup>

In the most recent event, an influenza strain with a combination of gene segments not previously reported in the swine or human influenza virus strains was identified firstly in Mexico and then in the United States of America.<sup>6</sup>

## Types

Influenza viruses are divided into 3 main types: A, B, and C. Most of the epidemics and outbreaks of flu are caused by types A and B, with type C being generally responsible for sporadic mild upper respiratory symptoms. The current vaccine includes three strains: two influenza A strains (H3N2 and H1N1) and one influenza B strain.

## Laboratory Investigation

Laboratory Investigation CDC performed genomic sequence analysis on all 18 specimens from infected humans; two different H3N2v viruses were identified. Among the 18 variant viruses detected in persons, 16 were reassortants, with a constellation of genes not previously detected in viruses infecting humans. Whereas these viruses contained seven gene segments similar to

segments detected in previously reported variant virus outbreaks, one gene segment coding for an influenza A(H3) hemagglutinin (HA) gene was determined to be similar to HA genes found in human seasonal influenza A(H3N2) viruses from 2010 and 2011. This HA gene was likely introduced from humans into swine in 2010 or 2011, and has since circulated and evolved in swine to be genetically and antigenically different from both previous and currently circulating human seasonal influenza A(H3N2) viruses (3). The viruses in the remaining two specimens had HA genes similar to those of swine-origin H3N2 influenza viruses circulating in the U.S. swine population since 1998, and previously identified in human H3N2v virus infections in the United States since 2009.<sup>7</sup>

### **Clinical manifestations**

Influenza typically begins with the abrupt onset of symptoms following an incubation period of 1 to 2 days. Primarily, these symptoms are systemic and consist of fever sensation, true chills, headache, severe myalgia, malaise, and anorexia. Symptoms of H3N2v infection are similar to those of seasonal flu viruses and can include fever and respiratory symptoms, such as cough and runny nose, and possibly other symptoms, such as body aches, nausea, vomiting, or diarrhea." In the early days, the patient has high-grade fever and on the 2nd and 3rd days, the fever decreases and diminishes gradually. It may, nonetheless, last for 4 to 8 days. Early in the course of the disease, the patient's face is plethoric with watery and red eyes. A convalescent period of some weeks may ensue, during which dry cough and malaise are the most salient complaints of the patient.<sup>8</sup>

### **Risk of influenza complications<sup>9</sup>**

1. Unvaccinated infants aged 12–24 months.
2. Persons with asthma or other chronic pulmonary diseases such as cystic fibrosis in children or chronic obstructive pulmonary disease in adults.
3. Persons with hemodynamically significant cardiac disease.
4. Persons who have immunosuppressive disorders or who are receiving immunosuppressive therapy HIV infected persons.
5. Persons with sickle-cell anemia and other hemoglobinopathies.
6. Persons with diseases requiring long-term aspirin therapy such as rheumatoid arthritis.
7. Persons with chronic renal dysfunction.
8. Persons with chronic metabolic diseases such as diabetes mellitus Persons with neuromuscular disorders, seizure disorders, or cognitive dysfunction which may compromise the handling of respiratory secretions.

**Prevention**

H3N2 infection can be prevented by wearing masks, avoiding crowded places, covering mouth and nose while sneezing and coughing, avoiding touching eyes and nose, especially after touching an external surface, drinking plenty of fluids, and taking paracetamol for fever and body ache.

Also, people must avoid shaking hands, must not spit in public, should not eat together sitting close to others, and must not take antibiotics or other medicines without consulting a healthcare professional.

Vaccination is the most effective way to prevent seasonal influenza infection. When the circulating viruses are well-matched with viruses contained in vaccines, an influenza vaccine is the most effective.

A trivalent influenza vaccine includes two subtypes of Influenza A virus, and one Influenza B virus subtype. Quadrivalent vaccines include all these viruses, along with another Influenza B virus subtype.

“Prevention measures, such as getting an annual flu vaccine, practicing good hand hygiene, and avoiding close contact with sick individuals and wearing masks are important to reduce the spread of H3N2 and minimize the risk of infection,”

**Treatment**

The first opportunity to assess the effect of antiviral use during a pandemic occurred in 1968. In 1966, the Food and Drug Administration had approved amantadine for chemoprophylaxis of influenza A virus infection.<sup>10</sup> In 2019, EMA licensed intravenous (IV) zanamivir for severe influenza virus infection in children over 6 months as well as adults. Doctors may prescribe an antiviral medication, such as oseltamivir (Tamiflu).<sup>11</sup> When started within 48 hours after developing flu symptoms, antiviral medication can help to shorten the duration of illness and prevent complications from developing. The Indian Medical Association has advised people not to panic and avoid taking antibiotics like azithromycin and amoxicillin without consulting a doctor as this can result in antibiotic resistance.

**Traditional Medicinal Plants for Influenza**

Severe influenza virus infections may occur in healthy children with and without previously established risk factors.<sup>12</sup> This means the clinician must respond as soon as possible when a patient's illness seems to be progressing. Neuraminidase inhibitor (NAI) treatment has been shown to be effective at risk of severe complications. Medicinal plants are termed to be one of the easy sources to get antiviral drugs since they have a proven record for antiviral activity. India is where Siddha and Ayurveda medicines are common and the Traditional healers, spread all over the



country have immense knowledge in curing many human diseases by using medicinal plants .<sup>13</sup> Medicinal plants with a potential to cure can be taken up for scientific studies to see if it can combat viral diseases, with the hope of finding next generation drugs for influenza.

**Table 1: Name of the plant and their active ingredients used for Influenza.**<sup>14-27</sup>

Sl. No.	Plant Name	Active Ingredients
1	<i>Coscinium fenestratum</i>	It is the source of important isoquinoline alkaloids (berberine, palmatine, tetrahydropalmatine crebanine, jatrorrhizine, etc.)
2	<i>Trichopus zeylanicus</i>	<i>Trichopus zeylanicus</i> revealed the presence of various secondary metabolites such as phenolics, alkaloids, flavonoids, tannins, terpenoids, steroids glycosides, saponins etc.
3	<i>Eugenia singampattiana</i>	Compounds like flavanol glycosides, polyphenols, ellagic acids, gallic acids were reported earlier from various species of <i>Eugenia</i>
4	<i>Vitex altissima</i>	<i>Vitex negundo</i> Linn revealed the presence of volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids, flavones, glycosides, iridoid glycosides and stilbene derivative
5	<i>Strychnos minor</i>	Various compounds of different phytochemical categories especially alkaloids have been identified in different parts of this plant. Different parts of this plant are rich in indole alkaloids strychnine and brucine which are responsible for a wide range of therapeutic potential and toxicity as well.
6	<i>Diotacanthus albiflorus</i>	Phenolic compounds or polyphenols are one of the most frequent and widespread groups of substances in the world of plants. The bark comprises up to 20% of the dry weight of woody vascular plants and contains polysaccharides, lignin, suberin, suberan, tannins or phenolic acids
7	<i>Strychnos nux-vomica</i>	It contains strychnine and brucine as main constituents. Minor alkaloids present in the seeds are protostrychnine, vomicine, n-oxystrychnine, pseudostrychnine, isostrychnine, chlorogenic acid, and a glycoside
8	<i>Chloroxylon swietenia</i>	The various parts of <i>C. swietenia</i> contains different chemical substances these are mono and sesquiterpenes, phenolics, coumarins, alkaloids, lignans, sugars.
9	<i>Helicteres isora</i>	Phytochemical screening of crude extract and chloroform extract of the plant shows the presence of carbohydrates, saponin tannin, proteins, steroids, anthraquinon glycosides, cardiac glycosides, phenolic compounds, terpenoides, alkaloid salts, and free alkaloids
10	<i>Andrographis paniculata</i>	The herb contains diterpenoids, flavonoids and polyphenols as the major bioactive components. The diterpenoids are deoxyandrographolide, neoandrographolide, 14-deoxy-11,12-didehydroandrographide and isoandrographolide. The flavonoids are 5-hydroxy-7,8-dimethoxyflavone, 5-hydroxy-7,8,2',5'-tetramethoxyflavone, 5-hydroxy-7,8,2',3'-tetramethoxyflavone, 5-hydroxy-7,8,2'-trimethoxyflavone, 7-O-methylwogonin and 2'-methyl ether
11	<i>Wrightia tinctoria</i>	<i>Wrightia tinctoria</i> were found to contain two flavonoid glycosides Kaempferol 3-O-rhamnoside and Quercetin 3-O-sophoroside and two flavonoid aglycone Kaempferol and Quercetin.
12	<i>Cayratia pedata</i>	<i>Cayratia pedata</i> showed the presence of tannins, flavonoids, terpenoids, alkaloids, carbohydrate, saponins, steroids, quinines, phenols, proteins, oils and fats, phytosterols, coumarins and phlobatannins.
13	<i>Salacia oblonga</i>	<i>S. oblonga</i> contain active principles such as salacinol, kotalanol, kotalgenin-16-acetate, and many more. Salacinol and kotalanol are potent $\alpha$ -glucosidase

		inhibitors that competitively bind to $\alpha$ -glucosidases in the small intestine.
14	<i>Salacia reticulata</i>	<i>Salacia reticulata</i> contains triterpenes, hydrocarbons and sitosterol from roots and stem barks. It also contains mangiferin (MA), kotalanol, and salacinol.

## CONCLUSION

Influenza epidemics and pandemics impose a heavy socioeconomic burden on all societies. Inactivated influenza vaccines are always well-tolerated, with the most common side effect being burning pain at the injection site. In clinical trials, serious adverse events have been reported in <1% of the individuals vaccinated. Consequently, the vaccination policy in high-risk groups should be the priority in the battle against flu. The risk of the development of antiviral drug resistance should be considered if we opt to treat all patients who are labeled as suffering from flu. Individuals with suspected flue with severe disease such as those with signs and symptoms of lower respiratory tract infections (e.g., dyspnea, tachypnea, and low oxygen saturation) and those who have signs of rapid clinical deterioration or those at high risk of complications should receive antiviral therapy. In addition, a new look at antiviral chemoprophylaxis and its appropriate use may effect a reduction in morbidity and mortality allied to flu in high-risk groups. Further evaluation needs to be carried out on plant/ herbs to explore the hitherto unknown effects and their practical pharmacological and clinical applications, for the welfare of the mankind.

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