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Development of herbal formulation for swine flu

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Abstract

Swine flu, also called Hog or Pig Flu, is an infection caused by any one of the several types of Swine influenza virus (SIV) which is common throughout pig population worldwide. The term "influenza" derived from Italian word "influenza". H1N1 influenza or swine flu is a contagious disease that is caused by the influenza virus. Infection with the H1N1 influenza virus can result in severe illness and life threatening complications. The proposed work of formulating Herbal Swine Flu tablets by the addition of excipients and compressing it into a tablet dosage form as an attempt to minimize side effect as well as to improve immunoefficiency caused by H1N1 influenza virus. In another way, shorten the duration of infection. So, this herbal tablets useful as immune enhancer also useful as disease resistance.

Keywords: Swine flu, H1N1 influenza, life- threatening, common flu

1. Introduction

Swine flu is an acute respiratory disease caused by a small spheroid virus that belongs to the Influenza A virus group. Swine influenza virus is any strain of the influenza family of viruses that is endemic in pigs [1]. H1N1 virus is a swine flu virus and which contains the genetic material of swine, bird and human influenza virus. Swine flu, also known as Influenza (H1N1), pig influenza, swine flu, hog flu and pig flu is a new influenza virus causing illness in people [2]. It infect the respiratory tract and result in nasal secretions, a barking like cough, decreased appetite and listless behavior. The scientists call this a quadruple reassortant virus and hence this novel virus is named Influenza-A (H1N1) virus. Influenza H1N1 is a circulating seasonal influenza virus [3]. Currently available drugs like neuraminidase inhibitors such as Tamiflu (oseltamivir), Zanamivir like antivirals have potential and resistance problem. Therefore the prospects for the control of H1N1 by existing anti-viral drugs are limited. Everyone is getting a little concerned over the recent spread of a possible super flu, a swine flu that has the properties of avian flu and human influenza [5]. It is troublesome, but there are lots of remedies, either to prevent a viral infection in the first place or to minimize the effects and shorten the duration if you do get an infection [6]. Most natural remedies are available over the counter these days, but there are some herbal medicines that are only available through naturopathy. The possible drugs include existing remedial measures as practiced such as Neem, Giloy, Ginger, turmeric, pepper and holy basil. There are some antiviral & antibiotic remediations in herbal medicines, which are reported to successfully control swine flu [7]. The traditional medicinal plants possess various medicinal properties and are highly effective to treat virus borne diseases. Herbal extracts of herbs shows antimicrobial activities, remove toxins from blood and boost the immunity [8].

1.1 Pathophysiology

Influenza viruses and the 2009 pandemic virus the influenza viruses are enveloped viruses with segmented negative stranded RNA genomes [9]. They are classified in three genera – A, B and C. The influenza A viruses contain eight genome segments that encode ten different viral proteins, of which nine are part of the virus structure. These include the surface haemagglutinin (HA), neuraminidase (NA) and M2 ion channel proteins, the M1 matrix protein, the nucleocapsid protein (NP) that packages the RNA genome and the replication complex comprising the PA, PB1 and PB2 proteins [10].

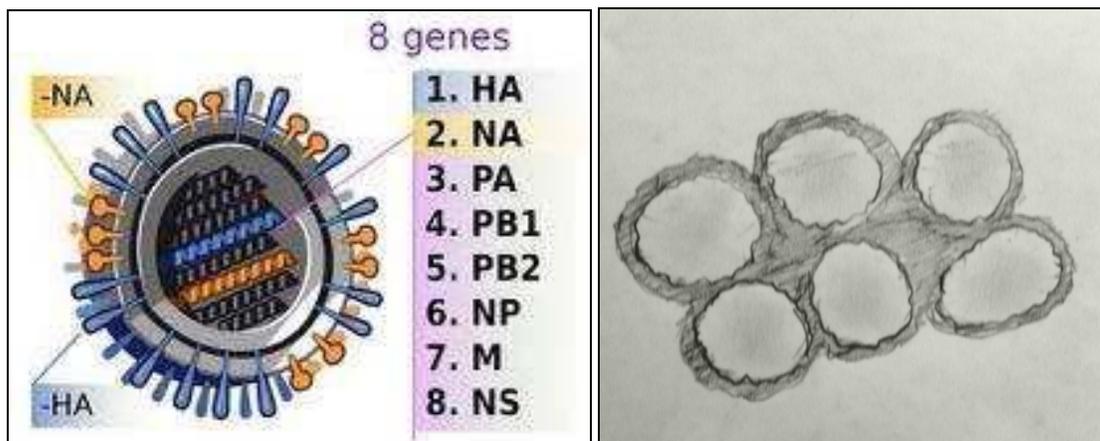


Fig 1: Electron microscopic image of H1N1 influenza virus

Some viruses also encode a protein called PB1-F2 from an alternate reading frame within the PB1 gene; this protein is also produced during infection and is associated with increased virulence and pathogenicity^[11]. Influenza viruses are named on the basis of their surface proteins –HA, which is required for virus binding to the target cell, and NA, which is required for virus release from infected cells. For influenza A viruses 16 HA serotypes (H1–H16) and 9 NA serotypes (N1–N9) are known, of which only the H1, H2, H3 and H5viruses, and rarely the H7 and H9 viruses have been found to infect humans^[12]. Influenza viruses evolve through antigenic drift, and occasionally by ‘antigenic shift. The viral RNA dependent RNA polymerase (replicase) lacks proofreading activity and is therefore unable to correct random errors introduced in the genome during replication. The effects of this are most obvious in the HA protein, which shows high rates of amino acid substitutions in its epitopes. And for which the ratio of non-synonym oustosynonymous substitutions is 1. This indicates a positive selection, which is directly related to evasion of host immunity. Antigenic drift changes the HA protein enough to render immunity acquired during an influenza season, either through infection or vaccination, ineffective in the next season^[14]. A more serious problem occurs when two different influenza viruses infect the same host. This leads to a reassortment of genome segments and the generation of novel progeny viruses^[15].

1.2 Sign and Symptoms^[16]

- Fever and extreme coldness (chills shivering, shaking (rigor))
- Cough and Nasal congestion
- Body aches, especially joints and throat
- Fatigue
- Headache
- Irritated, watering eyes
- Reddened eyes, skin (especially face), mouth, throat and nose
- Rapid Breathing or Difficulty in breathing
- Grayish or Bluish Skin Color
- Dehydration
- Persistent of severe vomiting
- Not able to interact properly with people, become irritable
- Flu like symptoms, bad cough and fever
- Shortness of breath or difficulty in breathing
- Pain in chest or abdomen
- Sudden dizziness or loss of energy
- Severe or continuous vomiting

Symptoms	Sensitivity	Specificity
Fever	68 – 86 %	25 – 73 %
Cough	84 -91 %	7 – 19 %

1.3 Treatment

Vaccination

Vaccines have been developed to protect against the virus that causes swine flu. There are two different brands of vaccine Pandemrix and Celvapan.

Antiviral therapy

Two classes of antiviral drugs are available for the prevention and treatment of influenza: neuraminidase inhibitors and adamantanes, which inhibit a viral protein called M2. Influenza as H1N1, formerly known as swine flu, has been found to be resistant to adamantanes (Amantadine and Rimantadine). Oseltamivir (Tami flu) and Zanamivir (Relenza) are the two neuraminidase inhibitors currently available^[17].

2. Need and Objective

2.1 Need

Currently available synthetic drugs are having potential and resistance problem. Therefore the prospects for the control of H1N1 by existing anti-viral drugs are limited. It is troublesome, but there are lots of remedies, either to prevent a viral infection in the first place or to minimize the effects and shorten the duration. The herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment.

The proposed project of formulating Herbal Swine Flu tablets by the addition of excipients and compressing it into a tablet dosage form by Direct Compression method is an attempt to minimize side effect as well as to improve immunoefficiency caused by H1N1 influenza virus. In another way, shorten the duration of infection. So, this herbal tablets useful as immune enhancer also useful as disease resistance. These tablets have the potential to be optimized for the, simplicity and cost effectiveness.

2.2 Objective

1. Preparation and optimization of Herbal Swine Flu Tablets.
2. Performance evaluation of Herbal Swine Flu Tablets.

3. Plan of Work

1. Selection of drug and excipients
2. Procurement of drug and excipients

3. Extraction Process
4. Preparation of Herbal Swine flu tablets
5. Evaluation of tablets
6. Result and discussion
7. Conclusion

4. Material and Equipments

4.1 Materials

4.2 Equipments

Table 1: List of materials Table

Sr. no	Name of the Materials
1	Giloy
2	Neem
3	Black Pepper
4	Tulsi (Bacilus)
5	Turmeric
6	Clove

Table 2: List of Equipments

Sr. no.	Name of the equipments
1	Digital Electronic balance
2	Monsanto hardness tester
3	Friability test apparatus
4	KBr Press
5	Hot air oven
6	Environmental test chamber
7	Centrifuge apparatus
8	Soxhlet Apparatus
9	Vernier Caliper

5. Experimental

5.1 Extraction of Piperine

Collection, identification

Black pepper (*Piper nigrum*) was arium specimen was deposited in Department of Pharmacognosy, Ashokrao Mane College of Pharmacy, Pethvadgaon for future referencing.

10g black pepper is ground to a fine powder and extracted with 150mL 95% ethanol in a Soxhlet extractor for 2hrs. The solution is filtered and concentrated in on a water bath at 60°C. 10ml 10% alcoholic KOH solution is added and after a while decanted from the insoluble residue. The alcoholic solution is left overnight, whereupon 0.3g yellow needles are deposited [18].

5.1.1 Characterization of piperine

Melting point

Melting point of the piperine was determined by using melting point apparatus.



Fig 2: Black Pepper

5.2 Extraction of Clove

150gm of ground clove (*Myratacae*) was followed by 2litres

of 80% ethanol to extract the phenolic compounds and sugars. The ethanol extract was concentrated on a evaporator and extracted three times with ethyl acetate to remove the phenolic compounds and polar organics. Finally the remaining ethanol solution was extracted three times with ethyl ether to remove the nonpolar organic compounds [19].



Fig 3: Clove

5.3 Neem Extraction

5.3.1 Oil extraction

Neem seeds were extracted using two solvent (n-hexane and ethanol) for 3 hours with ratio Neem seed powder to solvent volume of 1:5. In certain time intervals, the samples were taken and centrifuged to separate the solid fraction from solution. Filtrate was heated and evaporated to obtain solvent-free oil. Then the oil was weighed to calculate the concentration of oil in the solution. Extractions were conducted at 5 temperature level (30°, 35°, 40°, 45° and 50°C). [20]



Fig 4: Neem

5.4 Plant Collection and Extraction of Giloy

The formulation of Giloy Satva collected from market and fresh part of the (*Curculigo Orchiooides*). The powder of rhizomes was extracted by Maceration using Hydro alcoholic mixture for 72 hours. This extract was concentrated under vacuum and then subjected to preliminary photochemical screening [21].



Fig 5: Giloy

5.5 Preparation of Herbal Swine Flu Tablets

Giloy was taken in to mortar under continuous mixing all given quantity of ingredients add in to mortar with continuous trituration. The given powder mixture is poured in 12mm die. Then final mixture was compressed with pressure 2 ton, to

ensure tablet hardness around 4 kg/cm² with acceptable friability. Table 3 denotes the key formulation characteristics of Herbal Swine Flu tablets with different drug concentration and with excipients ratio respectively [22].

Table 3: Formulation table for Herbal Swine Flu tablets

HST System	Giloy (mg)	Neem (mg)	Turmeric (mg)	Clove (mg)	Tulsi (mg)	Black Pepper (mg)
HST 1	250	80	45	14	95	16
HST 2	280	40	45	30	80	25
HST 3	260	60	80	20	40	40
HST 4	200	100	30	15	150	05
HST 5	300	25	75	15	80	05



Fig 6: Herbal Tablets

5.5 Evaluation Tests

5.5.1 Weight variation test

Twenty tablets from each formulation were selected at random and average weight was determined. Then the individual tablets were weighed and were compared with average weight. Not more than 2 of individual weight deviate by more than percentage (refer table 4), while none deviates by more than twice that percentage [23]

Table 4: Uniformity of weight

Dosage form	Average weight	% deviation
Uncoated and film coated tablets	80 mg or less	10
	> 80mg and less than 250 mg	7.5
	250 mg or more	5

5.5.2 Hardness test

After preparation of matrices, primary micrometric properties are measured like, Tablet thickness, diameter, weight & hardness. Thickness & diameter is measured by using Vernier caliper, hardness is determined by using Monsanto hardness tester. Tablet hardness is defined as the force required breaking a tablet in a diametric compression force. It is also known as tablet crushing strength. The hardness tester used in the study was Monsanto Hardness Tester, which applies the force to the tablet diametrically with the help of an in built spring. The tester was initially adjusted to zero [24].

5.5.3 Diameter and thickness

Diameter and thickness was performed by using digital Vernier caliper. Results for all the batches of herbal tablets were reported.

5.5.4 Friability test

Friability test is performed to assess the effect of friction and shock that may often cause tablet to chip, cap, or break. Roche's friabilator was used for the purpose. Compressed tablets should not lose more than 1% of their weight (as per IP 96). It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability

of tablets was determined by using Roche's Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into Friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by [25].

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

(% Friability of tablets less than 1% is considered acceptable)

6. Result & Discussion

6.1 Extraction and characterization of piperine

Table 5: Extraction and Isolation of piperine

Extraction and Isolation	Observation
Piperine	Piperine was successfully isolated having yellow needles

6.1.1 Motic image for piperine



Fig 7: Motic image of piperine

6.1.2 Melting point

Melting point of Piperine was found to be 130 °C. The reported value for Piperine is 128-131 °C according to official monograph.

6.1.3 Solubility of piperine

Piperine was found to be soluble in ethanol, methanol and slightly soluble in water and PEG 400.

6.2 Evaluation of Herbal Tablets

6.2.1 Diameter, thickness, hardness and weight variation

The results of diameter, thickness, hardness and weight variation for all the batches of herbal tablets are shown in Table 6.

Table 6: Evaluation of herbal tablets

Formulation	Diameter (mm)	Thickness (mm)	Hardness (kg/cm ²)	Weight Variation (mg)
HST 1	13.12 ± 0.145	3.15 ± 0.01	4.1	462.30 ± 0.161
HST2	13.15±0.173	3.31±0.021	4.3	468.13±0.098
HST-3	13.17±0.251	3.35±0.017	4.5	471.23±0.224
HST-4	13.20±0.284	3.51±0.036	4.9	486.02±0.192
HST 5	13.19±0.392	3.40±0.029	4.6	482.32±0.346

*All readings are average ± SD (n=3)

6.2.2 Friability

The results of friability for all the batches of herbal tablets are shown in Table 7

Table 7: Evaluation of herbal tablets

Formulation	Friability (%)
HST 1	0.095 ± 0.007
HST 2	0.126 ± 0.003
HST3	0.089 ± 0.002
HST4	0.072 ± 0.006
HST5	0.274 ± 0.008

*All readings are average ± SD (n=3)

7. Summary and Conclusion

Summary

Some key findings from my research project are:

- Extraction of Black Pepper, Clove and Neem was carried out successfully.
- Characterization and identification of all herbal excipients was done.
- The Herbal tablets were prepared by direct compression method.
- Post compression study like Hardness, Thickness, Diameter, Friability and Weight variation of tablet is carried out.
- The optimized batch HST-4 passes all Post compression evolutionary tests.

7.1 Conclusion

According to Ayurveda, swine flu is placed under a class of diseases called Sannipatajvar. Sannipatajvar is basically triggered by an aggravation of the three Doshas (Vata, Pitta & Kapha) and a loss of Ojas in the body. Low Ojas is lack of immunity at the physical level and absence of mental strength at the mind level. By strengthening the Ojas you can easily prevent diseases like swine flu from attacking. Now days it has necessary that turn attention towards herbal therapy. The proposed project of formulating Herbal Swine Flu tablets by the addition of excipients and compressing it into a tablet dosage form as an attempt to minimize side effect as well as to improve immunoefficiency caused by H1N1 influenza virus. In another way, shorten the duration of infection. So, this herbal tablets useful as immune enhancer also useful as disease resistance. These tablets have the potential to be optimized for the, simplicity and cost effectiveness. Herbal tablets are prepared by direct compression method was evaluated successfully.

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