ejpmr, 2020,7(6), 760-765

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

ANTI-VIRAL (ANTI-FLU), ANTI-BACTERIAL IMMUNOBOOSTING ORAL COMPOSITION OF HERBAL EXTRACTS FOR TREATING RESPIRATORY INFECTIONS – A CASE STUDY

Rajesh Biswas*[1], Kakoli Biswas[2], Parikshit Bansal[3] and Shashi Gupta[4]

[1]Head, Zoology Department, Government Home Science College, Sector-10, Candigarh-160011, India.
[2]Head, Department of Biotechnology, DAV College, Sector-10, Candigarh-160011, India.
[3]Principal Scientific Advisor, Amulya Research Center (ARC), Amulya Herbs Pvt. Ltd., Plot No 293, Industrial Area, Phase-1, Panchkula, Haryana, India.
[4]Ayurvedic Consultant, Ayusham Health Care, Amulya Herbs Pvt. Ltd., Plot No 293, Industrial Area, Phase-1, Panchkula, Haryana, India.

***Corresponding Author: Dr. Rajesh Biswas**

Head, Zoology Department, Government Home Science College, Sector-10, Candigarh-160011, India.

Article Received on 01/04/2020 **Article Revised on 22/04/2020** **Article Accepted on 12/05/2020**

ABSTRACT

Few antiviral and a large number of antibacterial synthetic drugs are approved worldwide for treatment of respiratory infections caused by viruses and bacteria. Though the antiviral, antibacterial and immunoboosting properties of several herbs are well-documented, not a single standardized, herbal composition is approved globally for treatment of viral or bacterial respiratory infections. The present case discloses clinical results of a unique, standardized herbal extract formulation for treatment of respiratory tract infections, which offers potential for therapeutic and prophylactic use at global level, especially in epidemics. The formulation is a synergistic composition of alcoholic extracts of seven herbs *viz. C. longa (95% Curcumim) 26-31%; B. serrata (65% Boswellic acid) - 22-27%; M. pterygosperma - 18-23%; O. sanctum -7-12%; T. cordifolia- 7-12%; W. somnifera- 5-7%; P. nigrum (95% Piperine) - 1-2%*. Presentation of the composition is in form of capsules of 700 mg each for oral intake (Patent filed- Indian patent no. 202011016778 dt. 19/04/2020; International PCT Application No. PCT/IN2020/050448 dt. 19/5/2020) The composition was evaluated for therapeutic efficacy in six patients in age group of 15-57 years who were clinically diagnosed as suffering from viral infection (flu) or mixed respiratory infections caused by viruses and bacteria. Diagnosis and treatment was carried out by a Practising Ayurvedic Physician at Ayusham Health Care, an Ayurvedic Clinic based at Plot No 293, Industrial area, Phase-1, Panchkula, Haryana, India. When given orally to the patients at a dose of 2 capsules of 700 mg each, thrice a day (4.2 gm/day), the composition was very effective in rendering all patients asymptomatic within 2-3 days. Treatment was however continued for 7 days to ensure complete recovery and prevent relapse. No side-effects were observed in any of the patients. The present case study suggests that the powerful antiviral, antibacterial, anti-inflammatory, immunomodulator activity of the composition is due to the synergistic effect of 50-60 powerful phytochemicals which act as the biologically active components. The composition offers an affordable and effective treatment for upper respiratory tract infections (common cold, sore throat etc.) caused due to viral infections (flu) or mixed viral and bacterial infections. Possibilities of effectiveness of the composition needs to be explored against novel viruses causing epidemics such as 'Severe Acute Respiratory Syndrome (SARS)', 'Middle East respiratory syndrome (MERS)' and COVID-19.

KEYWORDS: anti-virus, antibacterial, herbal composition, respiratory infection, flu.

INTRODUCTION

Common Cold and Flu are the two most common respiratory diseases caused by viruses. In addition to viruses, bacteria also cause infections of the respiratory tract, making diagnosis and treatment of these respiratory infections tough and at times expensive. Immuno-compromised individuals, suffering from HIV or cancer undergoing chemotherapy/radiotherapy, patients who have undergone organ transplant and are on immunosuppressant drugs, are more prone to viral and bacterial infections. Livestock like poultry, pigs, sheep, goat, etc. reared for meat are also prone to respiratory infections in which the infection can travel to humans and lead to mass spread i.e. epidemic and pandemic.

Common Cold and Flu infect millions of people worldwide, every year. Because cold and flu share many similar symptoms, it can be difficult (or even impossible)

to tell the difference between them based on symptoms alone. They cannot be treated with antibiotics because antibiotics don't work against viruses. Flu is more severe than common cold and if left untreated, can lead to hospitalization in some cases.[1]

Viruses Causing Common Cold

There are more than 200 viruses which cause common cold, due to which a single 'anti-cold' vaccine is not possible. Even existing viruses keep on mutating and are not stable. Viruses causing common cold are **rhinovirus** which are responsible for up to 80% colds during peak season and 30%-40% of all adult colds. Other cold causing viruses include **coronavirus**, adenovirus, respiratory syncytial virus and parainfluenza virus. This is the reason why common cold remains 'uncontrolled' and occurs several times a year globally.[2,3,4]

Coronaviruses are a category of harmless, common cold causing RNA viruses found throughout the world. They are 'zoonotic' meaning they can spread from animals to humans and take more virulent forms. In past 20 years, three coronavirus outbreaks namely, "Severe Acute Respiratory Syndrome (SARS)" in 2002, "Middle East respiratory syndrome (MERS)" in 2012 and "COVID-19" in 2019, arising from bat-to-human transmission have taken place. Both SARS and MERS had higher mortality rates than COVID-19 but spread through human-human transmission more slowly. Soon after COVID-19 emerged, the new coronavirus, which is closely related to SARS, was recognized as its cause.[5,6,7,8] In recent years, more virulent strains of coronaviruses have emerged causing severe disease and death in humans.

Flu causing Viruses

There are three types of Influenza causing Viruses, A, B, C. Influenza causing virus subtypes are distinguished based upon the antigenic properties of two surface glycoproteins: hemagglutinin (H) and neuraminidase (N), which promote and coordinate host cell entry and exit, respectively. The United States Centers for Disease Control and Prevention identifies 18 H subtypes and 11 N subtypes, for a theoretical total of 198 strain variations.[9] However, only H1, H2, and H3 are known to have achieved substantial human-to-human transmission.[10]

Mutation in influenza viruses cause pandemics

Flu in humans is caused by influenza virus A and B types only. While types A and B are responsible for the majority of morbidity and mortality, type A is the only one with pandemic potential. This is because type A is the only strain with an animal reservoir. Aquatic birds and swine are important reservoirs for influenza A virus, which makes it tough to eradicate it while providing opportunities for viral mutation and re-assortment. Mixing can take place in 'birds', 'humans', 'swine' and transmission between bird to bird, bird to human, human to swine, swine to bird and so on, resulting in a 'cocktail' that is lethal to humans.[11] The genetic material of influenza virus being highly variable in nature, prevents maintenance of an adequate immune response acquired from previous infections, leading to annual epidemics of "seasonal influenza". Within the past one hundred years, four pandemics namely Spanish flu (1918-1920) caused by H1N1, Asian flu (1957–1958) caused by H2N2, Hong Kong flu (1968-1970) caused by H3N2 and Swine flu (2009-2010) caused by H1N1, have resulted from the emergence of a novel influenza strain[12] which killed millions of human beings worldwide.

Limitations of Existing Approaches for Prevention and Treatment of Viral Respiratory Infections

Existing approaches for prevention and treatment of viral respiratory infections include giving immunity boosting vitamins and minerals and use of vaccines and anti-viral drugs.[12,13,14,15,16] Though vaccines and antiviral drugs are powerful tools against flu, but they fail in case viruses mutate or flu is caused by viruses other than those used in the vaccine preparation.[12,13,14,15,16] Influenza virus, a RNA virus is prone to mutations during reproduction and is not genetically stable. Every generation is slightly different, and those differences accumulate as time passes. This slow deviation is called antigenic drift, and is the reason why it is necessary to reformulate flu vaccines every year.[17]

Reassortment is another significant way for viruses to evolve and create a new pandemic strain. For instance, if a human H3N2 flu virus and a bird H7N3 flu virus infect a person, reassortment can intermingle genes from both viruses during replication.[12] Reassortment among subtypes from avian and human viruses, produced new strains in 1957 (H2N2 subtype) and in 1968 (H3N2 subtype) human influenza pandemics. Several investigators have found influenza viruses that arose from triple reassortment events among swine.[17] Genetic sequence analysis of many viral subtypes suggested that the 2009 pandemic swine influenza virus arose from a reassortment event between a triple reassortant influenza virus containing human, swine, and avian influenza genes and a Eurasian swine influenza virus.[18] Mutation and change in structure of viruses causing respiratory diseases (e.g. cold, flu etc.) is a natural phenomenon and cannot be prevented. This underlines the need for a radically different approach to tackle the menace of respiratory infections caused by viruses, which affect people worldwide, since existing approaches have failed.

Limitations of Existing Approaches for Prevention and Treatment of Bacterial Respiratory Infections

Respiratory infections can also be caused by bacteria and leads to sore throat (pharyngitis also called tonsillitis because it leads to inflammation of the tonsils). In cases of infectious pharyngitis that are not viral, the cause is almost always a bacterium, usually a group A beta-hemolytic Streptococcus, which causes what is commonly called strep throat. Like viral pharyngitis, strep throat can spread quickly and easily within a

community, especially during late winter and early spring. Bacterial infections are treated by prescribing an antibiotic[19] or a broad-spectrum antibiotic.[20] Both antivirals and antibiotic drugs are associated with side effects such as, nausea and vomiting, bronchospasm, diarrhea, rash, dizziness and yeast infections.[21,22] Limitations of existing methods for the treatment of respiratory infections caused by viruses or bacteria or both, makes it important to search for alternative treatment.

New Approaches for Treatment- Fighting Nature with Nature

A wide variety of herbs are present in nature, with potent anti-viral and anti-bacterial activities. Ganjhu et al., have extensively reviewed the anti-viral activities of plants existing in nature.[23] The anti-viral activity of plants have also been extensively reviewed by Mukhtar et al.[24] Mohoti et al., have disclosed widespread antimicrobial activity of several plants found in Sri Lanka.[25] Use of Medicinal Plants as microbial agents, has been extensively reviewed by Parmar & Rawat.[26] Use of plants and herbs as immunity boosting agents have been reviewed extensively by Sultan.[27] Fighting 'Nature with Nature' approach against viruses and bacteria finds strong scientific support in published literature. Herbal plants, plant preparations and phytoconstituents have proved useful in attenuating infectious conditions and were the only remedies available, till the advent of antibiotics (many being of plant origin themselves). Among infectious diseases, viral diseases in particular, remain the leading cause of death in humans globally. Herbal sources provide researchers enormous scope to explore and bring out viable alternatives against viral diseases, considering non-availability of suitable drug candidates and increasing resistance to existing drug molecules for many emerging and re-emerging viral diseases.[23]

The present composition was developed to address the problem of viral infections (e.g. flu, common cold, sore throat etc.) and also bacterial infections in a single oral dosage form simultaneously, thus avoiding the need for separate antivirals and separate antibiotics. The present study was undertaken to evaluate its therapeutic efficacy and safety in patients diagnosed as suffering from upper tract respiratory infections caused by viral or bacterial infection.

MATERIALS AND METHODS

Ingredients of the composition (Patent filed- Indian patent no. TEMP/E-1/18246/2020-DEL; International patent no. PCT/IN2020/050367)

The composition consists of seven herbal extracts present in specific concentrations/ratios as given in Table 1 below:

Table 1: Ingredients of the antiviral, antibacterial, immunoboosting composition.

S. No.	Scientific Name of the Herb	Part of Herb used	Quantity (%) Of Alcoholic Extract	Quantity (mg) Of Alcoholic Extract	Bhava Prakash Nighantu[28] (BPN) page No
1.	*Curcuma longa* (95% Curcumim)	Rhizome	26-31%, optimal 28.5%	200mg	BPN111
2.	*Boswellia serrata* (65% Boswellic acid)	Resin	22-27%, optimal 24.5%	170mg	BPN712
3.	*Moringa pterygosperma*	Bark/Leaves	18-23%, optimal 20.5%	145mg	BPN324
4.	*Ocimum sanctum*	Leaves	7-12%, optimal 9.5%	66mg	BPN359, BPN496
5.	*Tinospora cordifolia*	Stem	7-12%, optimal 9.5%	66mg	BPN258
6.	*Withania somnifera*	Roots/Leaves	5-7%, optimal 6%	43mg	BPN379, BPN500
7.	*Piper nigrum (95% Piperine)*	Fruit	1-2%, optimal 1.5%	10mg	BPN12,BPN19
		Total	**100%**	**700mg**	

Method of Preparation

The Alcoholic extracts of the following herbs were taken in dried, fine powder form and blended: *Curcuma longa* (95% Curcumim) -200 mg, *Boswellia serrata* (65% Boswellic acid)- 170 mg, *Moringa pterygosperma*-145 mg, *Ocimum sanctum*- 66mg, *Tinospora cordifolia*-66 mg, *Withania somnifera*-43 mg and *Piper nigrum* (95% Piperine) - 10 mg. The fine blend was filled into capsules to give a single oral dosage form of 700 mg each. A small batch of 500 grams was prepared inhouse and around 700 capsules filled under supervision of the physician.

Details of Subjects

Six patients aged between 15 to 56 were examined by a practicing Ayurvedic Physician at Ayusham Ayurveda Clinic of Amulya Herbs Pvt. Ltd., Panchkula, Haryana, India. Based on the symptoms, they were clinically diagnosed as suffering from viral infection (flu) or mixed viral and bacterial infection. Details of the Subjects and

Signs and Symptoms on basis of which clinical diagnosis was carried out is given in Table 2 below.

Table 2: Details of Subjects and Clinical Diagnosis.

PATIENT DETAILS	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6
Age (Years)	15	24	56	53	53	49
Sex	Male	Female	Male	Female	Male	Female
Body Weight (Kg)	51	48	71	62	78	53
Treatment dates	16-22 Jan 2020	18-24 Jan 2020	21-27 Jan 2020	28Jan- 3 Feb, 2020	8-14th Mar,2020	3-12th Mar 2020
SIGNS & SYMPTOMS						
1. Symptom onset	Rapid	Rapid	Rapid	Rapid	Rapid	Rapid
2. Fever, °F Range	Yes 100-101	Yes 100-101	Yes 100-101	Yes 100-101	Yes 99-100	Yes 99-100
3. Body Aches	Yes	Yes	Yes	Yes	No	Yes, Severe
4. Chills	Yes	Yes	Yes	Yes	No	No
5. Fatigue, Weakness	Yes	Yes	Yes	Yes	No	Yes, Severe
6. Headache	No	No	No	No	No	Yes, Severe
7. Chest Discomfort	Yes	Yes	Yes	Yes	No	Yes, Severe
8. Cough	Mild	Mild	Mild	Mild	Mild	Severe
9. Stuffy /Runny Nose	Yes	Yes	Yes	Yes	No	No
10. Sore Throat	Yes	Yes	Yes	Yes	Yes	Yes
11. Difficulty in swallowing	Yes	Yes	No	Yes	No	Yes
12. Sneezing	No	No	No	No	No	No
13. Breathlessness	No	No	No	No	No	Yes
Physician Diagnosis	Viral Infection Flu	Viral Infection Flu	Viral Infection Flu	Viral Infection Flu	Bacterial Infection	Viral and Bacterial Infection

Recommended Dose and Duration of Treatment

Subjects were provided the composition in form of oral dosage form of capsules of 700 mg each. The dose recommended for treatment was 2 capsules of 700 mg each, thrice a day after meals for one week.

RESULTS

Details of Clinical outcome are given in **Table 3** below.

Table 3: Clinical results of Composition in Patients with Respiratory Infection.

	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6
Clinical Diagnosis	Viral Infection Flu	Viral Infection Flu	Viral Infection Flu	Viral Infection Flu	Bacterial infection	Flu, Secondary Bacterial Infection
Therapy*	2 caps, thrice a day, 7 days	2 caps, thrice a day, 7 days	2 caps, thrice a day, 7 days	2 caps, thrice a day, 7 days	2 caps, thrice a day, 7 days	2 caps, thrice a day, 10 days
Side-effects	NIL	NIL	NIL	NIL	NIL	NIL
Clinical Outcome	No Fever after 24 hrs. Asympto-matic after 3 days.	No Fever after 24 hrs. Asympto-matic after 3 days.	No Fever after 24 hrs. Asympto-matic after 3 days.	No Fever after 24 hrs. Asympto-matic after 4 days.	Fever gone after 24 hours. Asympto-matic after 2 days.	Fever and body ache gone after 24 hrs. Breath-lessness persisted.

**Composition was continued for 7 days in all patients, to ensure complete elimination of any infection and prevent relapse. In case of 6th patient, therapy was continued for 10 days. Breathlessness persisted in case of 6th patient and she was diagnosed as suffering from asthma. On treatment with medicines for asthma, patient got cured in due course of time.*

DISCUSSION

The case study has demonstrated the successful treatment of patients suffering from viral infections (e.g. flu, common cold, sore throat etc.) and bacterial infections, by using the composition in a single oral dosage form, thus avoiding the need for separate antivirals and antibiotics. The composition was very effective in treating respiratory infections caused by viruses and bacteria. The herbal composition uses extracts of herbs already in use as food or medicine, making it safe for use

as oral medicine.[23,24,25,26,27,28] This is not possible in case of new synthetic compounds which require very vigorous toxicity testing before their use can be permitted as medicine. Further, unlike existing synthetic anti-viral drugs and antibiotics, the herbal composition was totally free from any side-effects or undesirable effects. Owing to broad spectrum of activity against viruses and bacteria and also powerful immunoboosting properties, the composition provided quick relief. Evidence in support of the biological activities viz. anti-viral activity, anti-bacterial activity and immunobooster effect can be attributed to the specific ingredients of the composition and is well documented.[23,24,25,26,27]

The present composition does not contain any 'purified molecules' or single 'compound' at all. Rather, it is a very unique cocktail of more than 50-60 phytochemicals present in the standardized extracts of seven herbs which make up the composition. It is not possible for bacteria to develop resistance against this composition because resistance is developed against a single compound (antibiotic). When confronted with a complex mixture of molecules present in a polyherbal composition, bacteria fail to develop resistance and get killed. This is the reason why natural products documented in ancient texts hundreds of years old, still work and bacteria have been unable to develop resistance against them. Secondly, several of the phytochemicals have very powerful anti-viral activity and totally annihilate a wide variety of viruses. The composition was effective in treating viral infection in the present study, possibly because of those powerful phytochemicals effective against viruses causing flu, common cold, sore throat etc.

CONCLUSION

Present composition thus simultaneously performs the role of several 'anti-viral drugs', 'antibiotics' and 'immunoboosters' in a single oral dosage form, without any side effects. Use of standardized extracts eliminates batch to batch variation, ensures quality assurance of the product and approval by regulatory agencies and also easy clinical evaluation and correlation of results by clinicians and researchers across the world. The herbs used in the formula are all well-documented in global scientific literature in terms of safety and efficacy. Possibility of effectiveness of the present composition against novel zoonotic viruses originating due to mutation, antigenic drift and reassortment cannot be ignored. Therapeutic potential of the composition needs to be explored against "Severe Acute Respiratory Syndrome (SARS)", "Middle East respiratory syndrome (MERS)" and COVID-19.

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