



Available Online through

www.ijptonline.com

A STUDY ON IMMUNOSTIMULANT SUBSTANCES AND MEDICATIONS USED FOR TREATMENT OR PROPHYLAXIS OF SOME DISORDERS INCLUDING INFLUENZA INFECTIONS

Sameh Monir Abdou Desouki*

Clinical Pharmacy Specialist, Master in Clinical Pharmacy, Clinical Pharmacy Specialist at Sameh Pharmacy, Egypt.

Former Pharmacist in Gizan General Hospital, KSA.

Email: sammon2002@yahoo.com

Received on: 02-03-2019

Accepted on: 30-03-2020

Abstract:

Immunostimulants, some substances stimulate the immune system, have been used in the prevention and treatment of some diseases such as common cold and influenza. Also, there are herbal immunostimulants such as Echinacea, Garlic, and Ginseng which have been explored by many studies that have shown some results about using them in the treatment and prophylaxis of some diseases such as common cold and influenza. However, I failed to find studies that have explored any information about using these immunostimulant substances in the treatment and prophylaxis of other influenza virus infections, including H5N1, H1N1, SARS-CoV, and SARS-CoV-2. Therefore, I collected some related information from healthcare givers and adult people (via surveys) who experienced using of immunostimulant substances in treatment or prophylaxis in these diseases, to detect new results and data about them. Then, I explored some relevant positive results which are calculated and evaluated (with probability value $P < 0.05$). This study revealed some benefits about these issues; however, other studies should be conducted for clearer results.

Keywords: Echinacea, Immunostimulants, Herbal immunostimulants, H5N1, H1N1, SARS-CoV, SARS-CoV-2.

1. Introduction

Immunostimulants, some substances stimulate the immune system, have been used in the prevention and treatment of some diseases such as common cold and influenza. There are two types of immunostimulants [1]: specific and non-specific immunostimulants.

Specific immunostimulants stimulate an immune response to specific antigenic types such as vaccines or

Sameh Monir Abdou Desouki**et al.* /International Journal of Pharmacy & Technology
any antigen. On the other hand, non-specific immunostimulants such as female sex hormones, vitamin D, prolactin, and growth hormone, which do not have antigenic specificity, are widely used in chronic infections, autoimmunity, immunodeficiency, and neoplastic diseases [4,5]. They are known to stimulate both adaptive [2, 30] and innate immune responses [3].

Also, Immunostimulants that do not fit into these classes are categorized as other immunostimulants, like Immunostimulant herbs [6], also known as immunostimulators, have been used by billions of people, over thousands of years, in the treatment and prophylaxis of some diseases such as common cold, influenza, and some other viral infections[9,24]. These herbs stimulate the immune system to fight infections like colds and other viral inflammations [10]. For example, Goldenseal, Dong Quai, Maca Root, Astragalus root, Echinacea, Barley, Catnip, Coconut oil, Shiitake, Suma Root, Elderberry, Garlic, Ginseng, Kombucha, Maitake, Queen Of The Meadow, and Reishi [7,8] can stimulate the immune system via its components to enhance or boost the body's natural defense against illness and disease [11,12].

Echinacea (*Echinacea angustifolia*, *Echinacea purpurea*, *Echinacea pallida*) is commonly used, orally, to prevent colds and other respiratory tract infections, as it has an antiseptic, antiviral, and immune-stimulating effect. It can be used as monotherapy or in combination with other substances such as vitamins, herbs, minerals, or other immunostimulant substances. Also, Echinacea is a group of flowering plants used as a popular herbal remedy in reducing inflammation, improve immune response, lower blood sugar levels, and defend against oxidative stress [24]. As it can mobilize leukocytes, activate phagocytosis, and stimulate fibroblasts [14, 27, 28, 29].

The usual typical dose of *Echinacea purpurea*, for adult treatment, is a dry powdered extract (in capsules) that contains 300–500 mg USP of *Echinacea purpurea*, three times daily. While the therapeutic dose for children 1-4 years old is a liquid extract that contains 75–125 mg USP of *Echinacea purpurea*, 3-4 times daily. Also, the therapeutic dose for children 5-12 years old is a liquid extract that contains 150–250 mg USP of *Echinacea purpurea*, 3-4 times daily [25].

Echinacea purpurea has only a few reported severe side effects, such as abdominal pain, angioedema, dyspnea, nausea, pruritus, rash, erythema, and urticaria. However, it appears to be safe and well-tolerated in the short term, but its long-term effects are relatively unknown [26].

Despite there are many studies that have shown similar results about using immunostimulant herbs

Sameh Monir Abdou Desouki**et al.* /International Journal of Pharmacy & Technology (Especially *Echinacea purpurea*) in the treatment and prophylaxis of some diseases such as common cold and influenza [31,32,33], but I failed to find studies have explored any information about immunostimulant herbs (Especially *Echinacea purpurea*) or immunostimulant substances and their uses in the treatment and prophylaxis of the other influenza virus infections, including H5N1, H1N1, SARS-CoV, and SARS-CoV-2.

However, in aim to fill this gap, in this research, I collected, estimated and explored some important data (with probability value $P < 0.05$) about these issues, especially which concerned with using *Echinacea purpurea* (alone and with other substances) in treatment and prophylaxis of some diseases, including:

-Coronavirus disease 2019 (COVID-19): it is an infectious disease caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) [16].

-Swine influenza (influenza type A) is an infection (endemic in pigs, also called Spanish flu): it has several types like H1N1 and H1N2 [14].

-Severe acute respiratory syndrome (or SARS) is a disease caused by SARS-CoV.

-A bird-adapted strain of H5N1 called HPAI A(H5N1) for highly pathogenic avian influenza virus of type A of subtype H5N1 [13].

-Seasonal Influenza (the flu), is an infectious disease caused by an influenza virus (type A or B).

- Common cold.

- Upper and lower respiratory tract infectious diseases.

- Skin infectious diseases like minor wounds.

This study demonstrated many positive results and effects of the treatment and prophylaxis of these diseases.

However, It could be better if there are other newly conducted studies about these issues for stronger and clearer results.

2. Materials and Methods

In this research and during my work at hospitals (especially during: November 2010: March 2020), I noticed and collected some related data (by observation, face-to-face questioning and computerized questionnaires [17]) from professional healthcare givers (like physicians, nurses, specialists, general practitioners), adult people (with ages between 21-55 years old- about 90% of them from the Kingdom of Saudi Arabia and Egypt [18]) who had an experience with diseases and using of immunostimulant substances in treatment or prophylaxes in these diseases, especially *Echinacea purpurea*, and treatment and prophylaxis of some

Sameh Monir Abdou Desouki**et al.* /International Journal of Pharmacy & Technology diseases. They gave me all the required information without any identification data (like name or address) [19,20]. I collected these data as retrospective nominal or ordinal registered data [21,23] to be calculated and evaluated (with probability value $P < 0.05$) [22].

I tried to quantify my results and data as much as possible. So, I made a scale from 6 stages to determine the percent (and degree) of disease severity change or probability of infection attack or symptoms change after using the treatment regimen. They are 100%: 0%, 0 to -25%, -25 to -50%, -50 to -75%, and -75% to -100%. The negative numbers refer to the decreasing severity of the disease symptoms (in the case of treatment) or they refer to the degree of change in disease severity in the case of infection or infection probability (in the case of prophylaxis) in the following order: mild (0: -25%), moderate (-25: -50%), severe (-50: -75%), highly severe (-75%: -100%). The positive numbers refer to the opposite. Then, I calculated and listed the positive and negative results of each group in simple numbers and integrated percents.

Also, I used my laboratory to prepare a 5ml solution that contains 500 mg of *Echinacea purpurea* liquid extract, and I got some information about these issues from other references as well as the internet. Also, all medications used in all these studies are according to USP (The United States Pharmacopoeia).

3. Results

I tried to do new research about using of immunostimulant substances in treatment or prophylaxes in some diseases, especially which concerned with the treatment or prophylaxis of influenza viruses, including H5N1, H1N1, SARS-CoV, SARS-CoV-2. However, I evaluated and explored all these data about these issues with probability value $P < 0.05$.

3.1 The First Study

In treatment, using *Echinacea purpurea* (alone and with the usual typical recommended drug treatment regimen compared with the usual recommended drug treatment regimen alone) in healthy adult people, with a dose of 300–500 mg Capsules, (containing *Echinacea purpurea* powder) USP, three times daily for 7-14 days, starting from the first or second day of symptoms onset, in:

1- Common Cold treatment:

8 (about 20%) of 39 people said there is a reduction in the severity and duration of typical cold symptoms by about -25:-50% if *Echinacea purpurea* is used as therapy with the usual drug treatment regimen for 7-14 days starting from the first or second day of symptoms onset.

2- Influenza (type A or B) treatment:

10 (about 26%) of 38 people said there is a reduction in the severity and duration of typical influenza symptoms by about -25:-50% when *Echinacea purpurea* is used as therapy with the usual recommended drug treatment regimen for 7 to 14 days starting from the first or second day of symptoms beginning.

While in prophylaxis, using *Echinacea purpurea* in healthy adult people (who are not vaccinated with the influenza vaccine), with a dose of 300–500 mg Capsules (containing powder of *Echinacea purpurea*) USP, two times daily for 2-4 weeks, in:

3-Common Cold prophylaxis:

9 (about 36%) of 25 people said there is a reduction in the usual probability of a severe cold attack or severe symptoms (not mild or moderate attack or symptoms), by about -25:-50% when *Echinacea purpurea* is used as a monotherapy. And the prophylaxis has extended for 1-3 weeks after *Echinacea purpurea* administration has been stopped.

4-Influenza (type A or B) prophylaxis:

4 (about 40%) of 10 people said there is a reduction in the usual probability of severe influenza attack or severe infection (not mild or moderate attack or symptoms), by about -25:-50%, if *Echinacea purpurea* is used as a monotherapy. And the prophylaxis has extended for 2-6 weeks after *Echinacea purpurea* administration has been stopped.

Notice: Most of the people (about 85%) prefer influenza vaccines more than *Echinacea purpurea* administration for influenza prophylaxis.

We can see the results of prophylaxis clearer and more significant than these in treatment.

The results could be summarized in the following **table-1**.

	Treatment	Prophylaxis
Common Cold	8 of 39 (about=20%)	9 of 25 (about=36%)
Influenza type A or B	10 of 38 (about=26%)	4 of 10 (about=40%)
Treatment Course Period	7-14 days	2-4 weeks
Percent of Disease Severity Change	-25: -50%	-25:-50%

3.2 The Second Study

In treatment, using *Echinacea purpurea* in healthy adult people, with a dose of 300–500 mg capsules (containing *Echinacea purpurea* powder) USP, three times daily for 1-2 weeks, and in combination with other usual recommended drug treatment regimens and additive medications, all with ordinary therapeutic doses, starting from the first day or second day of symptoms onset compared to the usual recommended drug treatment regimen alone.

These additives should be in usual therapeutic effective doses, like:

-Multivitamins and Minerals, like Vitamin D, C, Zn, and other minerals

-Other immunostimulant drugs, like Garlic 150 - 1200 mg USP Capsules of aged garlic extract once daily, and Panax Ginseng 200-1000 mg USP Capsules daily.

-B2 receptor agonist as Salbutamol 2mg USP Tablets or syrup as needed

-Mucosolvent, as Bromohexine 4 mg USP Tablets or syrup 2-3 times daily

-Expectorant, as Guaifenesin 400 mg USP Capsules or syrup 4- 6 times daily

-Other hot drinks such as Ginger syrup or Mint syrup

The usual recommended drug treatment regimen may contain broad-spectrum antibiotics and safety range, like azithromycin 500mg (USP) Capsules, one capsule every day for 3 days, or even using a more broad-spectrum antibiotic according to the case situation and treatment guidelines.

So, the whole course of treatment will be *Echinacea purpurea* + usual drug treatment regimen + the additive medications, and all with ordinary therapeutic doses, for 1-2 weeks starting from the first day or second day of symptoms onset.

1- Common Cold treatment:

8 (about 42%) of 19 people said there is a reduction in the severity and duration of typical cold symptoms by about -25:-50%, in comparison with using the usual drug therapy regimen alone.

2- Influenza (type A or B) treatment:

9 (about 45%) of 20 people said there is a reduction in the severity and duration of typical influenza symptoms by about -25:-50%, in comparison with using the usual drug therapy regimen alone.

3-Influenza (H5N1) treatment:

6 (about 37.5%) of 17 people said there is a reduction in the severity and duration of typical influenza

Sameh Monir Abdou Desouki*et al. /International Journal of Pharmacy & Technology
symptoms by about -25:-50%.

4- Influenza (H1N1) treatment

3 (about 33.3%) of 10 people said there is a reduction in the severity and duration of typical influenza symptoms by about -25:-50%.

5-Influenza (SARS-CoV) treatment:

2 people (as a reference sample group that used this combination of drugs only) said there is a reduction in the severity and duration of typical influenza symptoms by about -25:-50%.

6- Influenza (SARS-CoV-2) treatment:

18 people (no other people used this combination of drugs) said there is a reduction in the severity and duration of typical influenza symptoms by about -25:-50%.

While in prophylaxis, using *Echinacea purpurea* in healthy adult people, with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, two times daily for 1-3 weeks, in combination with some additives (including multivitamins and minerals, such as Vitamins D, and C, Zn Mineral and other minerals, and hot drinks like ginger syrup or mint syrup), in:

1-Common Cold prophylaxis:

4 (about 50%) of 8 people said there is a reduction in the usual probability of a severe cold attack or severe symptoms (not mild or moderate attack or symptoms), by about -50:-75%.

2-Influenza (type A or B) prophylaxis:

5 (about 36%) of 14 people said there is a reduction in the usual probability of severe influenza attack or severe infection (not mild or moderate attack or symptoms), by about -50:-75%.

3-Influenza (H5N1) prophylaxis:

8 people (no other people used this combination of drugs) said that they have a better immunity (as they have higher leukocytes), and feel slightly better in safety and trust.

4- Influenza (H1N1) prophylaxis:

4 people (no other available reference people group that used this combination of drugs) said that they have better immunity, and feel slightly better in safety and trust (as they have higher leukocytes).

5-Influenza (SARS-CoV) prophylaxis:

3 people (no other available people used this combination of drugs) said that they have better immunity, and

feel slightly better in safety and trust (as they have higher leukocytes).

6- Influenza (SARS-CoV-2) prophylaxis:

19 people (no other available reference group of people used this combination of drugs) said that they have better immunity, and feel slightly better in safety and trust (as they had higher leukocytes).

We can see the results of prophylaxis clearer and more significant than these in treatment.

We can see both results of prophylaxis and treatment are clear and significant than these in treatment. But less clear in the case of SARS-CoV and SARS-CoV2.

The results could be summarized in the following **table-2**.

	Treatment	Prophylaxis
Common Cold	8 of 19 (=about 42%)	4 of 8 (=about 50%)
Influenza type A or B	9 of 20 (=about 45%)	5 of 14 (=about 36%)
Influenza (H5N1)	6 of 17 (=about 35%)	8 people#
Influenza (H1N1)	3 of 10 (= about 30%)	4 people#
Influenza (SARS-CoV)	2 people#	3 people#
Influenza (SARS-CoV2)	18 people#	19 people#
Treatment Course Period	1-3 weeks	1-2 weeks
Percent of Disease Severity Change	-25:-50%,	-50:-75%###
# No other available reference group of people that used this combination of drugs		
###50:-75%: in Common Cold and common Influenza (type A or B) only		

3.3 The Third Study

These data are about children and adults with some chronic diseases (like patients with: chronic kidney failure, diabetes mellitus disease, and hypertension) or adults over 60 years old.

For Treatment, the usual dose (for the adults) of *Echinacea purpurea*, is a dry powdered extract (in capsules) that contains 300–500 mg USP of *Echinacea purpurea*, three times daily, for 7-14 days

While the therapeutic dose for children 1-4 years old is a liquid extract that contains 75–125 mg of *Echinacea purpurea*, 3-4 times daily, for 7-14 days

While the therapeutic dose for children 5-12 years old is a liquid extract that contains 150–250 mg of

The above *Echinacea purpurea* regimens were administered as a monotherapy along with the usual recommended drug treatment regimen, for 7-14 days starting from the first day or second day of symptoms onset in comparison with the usual recommended drug treatment regimen alone.

1- Common Cold treatment:

People said there is a reduction in the severity and duration of the typical symptoms by about -25:-50%, when *Echinacea purpurea* is used as monotherapy along with the usual recommended drug treatment regimen, starting from the first or second day of the onset of symptoms:

-For children 1-4 years: 5 of 22 (about 22%)

-For children 5-12 years: 6 of 26 (about 23%)

-For the adults with some chronic diseases or adult over 60 years old: 8 from 31 (about 26%)

2- Influenza (type A or B) treatment:

People said there is a reduction in the severity and duration of the typical cold symptoms by about -25:-50%:

-For children 1-4 years: 4 of 16 (about 25%)

-For children 5-12 years: 6 of 21 (about 28%)

-For adults with some chronic diseases or adults over 60 years old: 7 of 26 (about 27%).

While in prophylaxis, by the usual dose of *Echinacea purpurea*:

-For the adults, it is a dry powdered extract (in capsules) that contains 300–500 mg USP of *Echinacea purpurea*, two times daily, for 7-14 days.

-For children 1-4 years old, it is a liquid extract that contains 75–125 mg USP of *Echinacea purpurea*, two times daily, for 7-14 days

-For children 5-12 years old, it is a liquid extract that contains 150–250 mg USP of *Echinacea purpurea*, two times daily, for 7-14 days.

The regimens above were administered (only treatment with *Echinacea purpurea* as monotherapy) for 1-2 weeks.

People said there is a reduction in the usual probability of cold attack or symptoms, by about -25:-50% in the case of common cold, and 25-50% in the case of influenza, while using *Echinacea purpurea* as a monotherapy. The prophylaxis extended for 1-3 weeks after the *Echinacea purpurea* administration was

stopped.

1-Common Cold prophylaxis:

-For children 1-4 years: 8 of 19 (about 42%)

-For children 5-12 years: 9 of 17 (about 52%)

-For adults with some chronic diseases or adult over 60 years old: 9 of 22 (about 41%)

2-Influenza (type A or B) prophylaxis:

-For children 1-4 years: 4 of 14(about 28.5%)

-For children 5-12 years: 5 of 16 (about 31%)

-For adults with some chronic diseases or adult over 60 years old: 4 of 13 (about 31%)

We can see the results of prophylaxis clearer and more significant than these in treatment.

The results could be summarized in the following **table-3**.

	Treatment	Prophylaxis
Common Cold		
-for children 1-4 years	5 of 22 (= about 22%)	8 of 19 (= about 42%)
-for children 5-12 years	6 of 26 (= about 23%)	9 of 17 (= about 52%)
-for the adults with some chronic diseases or adult over 60 years old	8 of 31 (= about 26%)	9 of 22 (= about 41%)
Influenza type A or B		
-for children 1-4 years	4 of 16 (= about 25%)	4 of 14 (= about 28%)
-for children 5-12 years	6 of 21 (= about 28%)	5 of 16 (= about 31%)
-for the adults with some chronic diseases or adult over 60 years old	7 of 26 (= about 27%)	4 of 13 (= about 31%)
Treatment Course Period	1-2 weeks	1-3 weeks
Percent of Disease Severity Change	-25:-50%	-25-50%

3.4 The Fourth Study

In treatment, use of some other immunostimulant drugs like coconut oil, garlic or ginseng along with the usual recommended drug treatment regimen with some additives.

So, the whole course of treatment will be: the other immunostimulant drugs + usual drug treatment regimen + additive medications, all with ordinary recommended therapeutic doses, for 1-2 weeks starting from the first day or second day of the onset of symptoms, in comparison with using of the usual drug treatment regimen (the regimen of treatment according to the corresponding disease treatment guidelines) alone.

1- Common Cold treatment:

38 (about 63%) of 60 people said there is a reduction in the severity and duration of the usual cold symptoms by about -25:-50%, in comparison to the use of the usual drug treatment regimen alone.

2- Influenza (type A or B) treatment:

29 (about 50%) of 58 people said there is a reduction in the severity and duration of the typical influenza symptoms by about -25:-50% while using *Echinacea purpurea* as therapy along with the usual drug treatment regimen, for 7 to 10 days starting for the first day of symptoms onset, in comparison with the use of the usual drug treatment regimen alone.

3-Influenza (H5N1) treatment:

10 (about 55%) of 18 people said there is a reduction in the severity and duration of the typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

4- Influenza (H1N1) treatment

8 (about 42%) of 19 people said there is a reduction in the severity and duration of the typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

5-Influenza (SARS-CoV) treatment:

8 (about 38%) people from 21 said there is a reduction in the severity and duration of the typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

6- Influenza (SARS-CoV-2) treatment:

21 (about 54%) of 39 people said there is a reduction in the severity and duration of the typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

While in prophylaxis, use of some other immunostimulant drugs, like garlic (250-1200 mg daily) or *Panax ginseng* (200-1000 mg daily) with some additives (as mentioned above), in:

1-Common Cold prophylaxis:

16 (about 64%) of 25 people said there is a reduction in the usual probability of cold attack or symptoms by

Sameh Monir Abdou Desouki*et al. /International Journal of Pharmacy & Technology
 about -50:-75% during the use of this regimen.

2-Influenza (type A or B) prophylaxis:

9 (about 32%) of 28 people said there is a reduction in the usual probability of influenza attack or infection, by about -25:-50%.

3-Influenza (H5N1) prophylaxis:

9 (about 19%) of 46people said that they have a better immunity (as they have slightly higher leukocytes and the patients feel slightly better in safety and trust.

4- Influenza (H1N1) prophylaxis:

7 (about 20%) of 35 people said that they have better immunity, and feel slightly better in safety and trust (as they have higher leukocytes and the patients feel better).

5-Influenza (SARS-CoV) prophylaxis

6 (about 15%) of 41 people said that they have better immunity, and feel slightly better in safety and trust. (as they have slightly higher leukocytes and the patients feel better).

6- Influenza (SARS-CoV-2) prophylaxis:

5 (about 13%) of 38 people said that they have better immunity, and feel slightly better in safety and trust. (as they have slightly higher leukocytes and the patient feel better).

We can see the results of treatment clearer and more significant than these in prophylaxis. Except in common cold as both of them are significant.

The results could be summarized in the following **table-4**.

	Treatment	Prophylaxis
Common Cold	38 of 60 (= about 63%)	16 of 25 (= about 64%)
Influenza type A or B	29 of 58 (= about 50%)	9 of 28 (= about 32%)
Influenza (H5N1)	10 of 18 (= about 55%)	9 of 46 (= about 19%)
Influenza (H1N1)	8 of 19 (= about 42%)	7 of 35 (= about 20%)
Influenza (SARS-CoV)	8 of 21 (= about 38%)	6 of 41(= about 15%)
Influenza (SARS-CoV2)	21 of 39 (= about 54%)	5 of 38 (= about 13%)
Treatment Course Period	1-3 weeks	1-2 weeks

Percent of Disease Severity Change	0:-25%.#	-50:-75%##
	-25:-50%#	-25:-50%.##

0:-25%: in influenza H5N1, H1N1, SARS-CoV, and SARS-CoV2.

and -25:-50%. for common cold and common Influenza (type A or B) only

##50:-75%: in common cold only

and -25:-50%. for common Influenza (type A or B) only

3.5 The Fifth Study

With other infectious diseases, using *Echinacea purpurea* (alone as a monotherapy along with the usual recommended drug treatment regimen) in healthy adult people, with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, three times daily for 7-14 days, in comparison with the use of the usual recommended drug treatment regimen alone, starting from the first day or second day of the onset of.

While in prophylaxis, 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, twice daily for 2-3 weeks as a prophylactic dose:

1-Skin infection (like Cellulitis and Minor wounds):

In treatment: 1 of 6 people said that there is a reduction in the severity and duration of symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

In prophylaxis: 2 of 8 people said there is a reduction in the usual probability of cold attack or symptoms, by about 0:-25%.

2-Upper respiratory infections:

In treatment: 10 of 25 people said that there is a reduction in the severity and duration of the typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

In prophylaxis: 17 of 26 people said there is a reduction in the usual probability of cold attack or symptoms, by about -25:-50%, in comparison with the use of the usual drug treatment regimen alone.

3-Lower respiratory infections:

In treatment: 2 of 11 people said that there is a reduction in the severity and duration of typical influenza symptoms by about 0:-25%, in comparison with the use of the usual drug treatment regimen alone.

In prophylaxis: 9 of 21 people said there is a reduction in the usual probability of cold attack or symptoms, by about 0:-25%.

We can see the results of prophylaxis clearer and more significant than these in treatment. Except in upper respiratory infection as both of them are significant.

The results could be summarized in the following **table-5**.

	Treatment	Prophylaxis
Skin infection and wounds	1 of 6 (=about 17%)	2 of 8 (=about 25%)
Upper respiratory infections	10 of 25 (=about 40%)	17 of 26 (=about 65%)
Lower respiratory infections	2 of 11 (=about 18%)	9 of 21 (=about 43%)
Treatment Course Period	1-2 weeks	2-3 weeks
Percent of Disease Severity Change	0:-25%. -25:-50%#	0:-25%. -25:-50%.#
# -25:-50%. for upper respiratory infections treatment only		

3.6 The Sixth Study

This study about the effect of other vaccines on other influenza infections, as vaccines considered as specific immunostimulants, stimulate immune responses to specific antigenic types, but there is no significant effect of vaccination on influenza treatment or prophylaxis, including vaccines that are related to respiratory tract infections, like pneumococcal polysaccharide vaccine which prevents pneumococcal bacteremia, and Influenza vaccines [35]. Bacille Calmette-Guérin (BCG) is a vaccine for tuberculosis (TB) disease (34).

But in some cases (vaccinated and living in sunny hot weather, about 27-35 degrees Celcius) of N1H5, H1N1 (Pigs, swine influenza viruses), SARS-CoV, or SARS-CoV-2. If the people vaccinated (more than 10 years before) with Bacille Calmette-Guérin (BCG), faster response with lesser disease symptoms in the degree (-0%:-25%) will be. I found that:

-in H5N1, only 4 of 23 people got a better response in the treatment.

-While in H1N1, only 3 of 19 people got a better response in the treatment.

-While in SARS-CoV, 7 of 21 people got a better response in the treatment

-While about 24 of 37 people show a much better response to treatment against SARS-CoV-2.

In spite the results show some significance but but this may attribute to other factors too, like sunny weather.

The results can be summarizing in the following **table-6**.

Character	Treatment
Influenza (H5N1)	4 of 23 (= about 17%)
Influenza (H1N1)	3 of 19 (= about 16%)
Influenza (SARS-CoV)	7 of 21 (= about 33%)
Influenza (SARS-CoV2)	24 of 37 (= about 64%)
Treatment Course Period	If the people vaccinated (more than 10 years before) with Bacille Calmette-Guérin (BCG).
Percent of Disease Severity Change	0:-25%.#

0:-25%: in influenza H5N1, H1N1, SARS-CoV, and SARS-CoV2.

If the people vaccinated (more than 10 years before) with Bacille Calmette-Guérin (BCG), and lived in sunny hot weather, about 27-35 degrees Celcius.

3.7 The seventh study

This study about *Echinacea Purpurea* side effects and safety, as *Echinacea purpurea* appears to be safe and well-tolerated in the short term like 1-2 weeks, but its long-term effects are relatively unsafe.

It was noticed that 5 of 29 people developed a skin rash and skin allergy (like erythema, and mild urticaria) after 2 weeks of the usual recommended dose administration. Then, another 3 of the 19 people after 4 weeks of the typical recommended dose administration.

This percent gradually increases with increasing duration of dose administration especially for more than 2 months, as percent and this enhances the probability of side effects occurring.

The results could be summarized in the following **table-7**.

Number of people who developed side effects	Period of administration
5 of 29 people (=about 40%)	14 days
3 of the 29 (=about 40%)	28 days
Total = 8 of 29 (= about 27%)	

3.8 The eighth study

This study about the relation between *Echinacea Purpurea* response and its dose, as the study, showed some significant results as in the followings:

I noticed that 7 children age 1-2 years old showed faster immune responses to the vaccine than other children by 25: 50% as 75-125 mg drops of *Echinacea purpurea* was administered to them, 3-7 days before their vaccine administration.

Also, it was noticed that 6 of 13 healthy adult people showed a faster increase in leukocytes through the first 1-2 weeks of administration of *Echinacea purpurea* 700-1000 mg USP, three times daily. Also, when I tested it in one case (on my self) before (5ml solution that contains 500 mg of *Echinacea purpurea* liquid extract, by intravenous injection every 24 hours for 3 days), I observed a more rapid response, but the rash appeared faster.

The results could be summarized in the following **table-8**.

People who showed faster immune responses	Number
Children age 1-2 years old	7#
Adults	6 of 13 (= about 46%)
## No other available reference group of people.	

4. Discussion

The main objectives of this paper are collecting new information about these issues from professional healthcare givers or adult people who have important information about, to estimate and explored using of immunostimulant substances in treatment or prophylaxes in some diseases, especially which concerned with the treatment or prophylaxis of influenza viruses, including H5N1, H1N1, SARS-CoV, SARS-CoV-2. However, this information can be discussed and interpreted as in the followings:

The first study: In prophylaxis, the results in using *Echinacea purpurea* in healthy adult people (who are not vaccinated with the influenza vaccine.), with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, two times daily for 2-4 weeks, for common cold prophylaxis and common influenza (type A or B), prophylaxis is clearer and more significant than that in the treatment regimen.

The second study: In treatment, using *Echinacea purpurea* in healthy adult people, with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, three times daily for 1-2 weeks, in combination with the usual drug treatment regimen and additive medications, and all with ordinary therapeutic doses, for 1-2 weeks starting from the first day or second day of symptoms onset. This gives better results than using the usual drug therapy regimen alone.

Also, in prophylaxis using *Echinacea purpurea* in healthy adult people, with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, two times daily for 1-3 weeks, in combination with some additives (including multivitamins and minerals, such as vitamins D, C, Zn, and hot drinks like ginger syrup or mint syrup). These additives have a positive effect on symptoms and in the treatment of cases as well as prophylaxis. But the results are much clearer and significant in treatment or prophylaxis of common cold, common influenza viruses, than those in H5N1, H1N1, SARS-CoV, and SARS-CoV-2.

The third study: These data are clearer and significant in children 5-12 years old, that are treated with a liquid extract that contains 150–250 mg USP of *Echinacea purpurea*, 3-4 times daily, for 7-14 days, than in children 1-4 years old treated with a liquid extract that contains 75–125 mg USP of *Echinacea purpurea*, 3-4 times daily, for 7-14 days, and in adults with some chronic diseases or adults over 60 years old.

The fourth study: Results of the treatment regimen, using the course of treatment that contains immunostimulant drugs + usual drug treatment regimen + addictive medications, all with ordinary recommended therapeutic doses, for 1-2 weeks starting from the first day or second day of symptoms onset, in comparison with the use of the usual drug treatment regimen (the regimen of treatment according to the corresponding disease treatment guidelines) alone. The results of treatment are clearer and significant than those in the prophylaxis regimen. Except in common cold and seasonal influenza as both results of treatment and prophylaxis are clear and significant.

The fifth study: In using *Echinacea purpurea* (alone as monotherapy with the usual recommended drug treatment regimen) in healthy adult people, with a dose of 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, three times daily for 7-14 days. While in prophylaxis, 300–500 mg Capsules (containing *Echinacea purpurea* powder) USP, twice daily for 2-3 weeks as a prophylactic dose, these results show some benefits in the prophylaxis of upper respiratory tract infections, and in its treatment too, but with a slightly less clear data. Also, the data evidence is slightly less clear in the prophylaxis of lower

Sameh Monir Abdou Desouki**et al.* /International Journal of Pharmacy & Technology
respiratory tract infection, while not much significant or clear in the treatment of lower respiratory tract system infection or skin diseases.

The sixth study: Vaccines considered as specific immunostimulants, stimulate immune responses to specific antigenic types, but there is no significant effect of vaccination on influenza treatment or prophylaxis, except some vaccines that are related to respiratory tract infections, especially Bacille Calmette-Guérin (BCG), also, the patients were living in sunny hot weather, about 27-35 Celsius. So, In spite the results show some significance but but this may attribute to other factors too, like sunny weather However, more studies needed to be conducted for more confirmation.

The seventh study: showed that *Echinacea Purpurea* appears to be safe and well-tolerated in the short term like 1-2 weeks, but its long-term use for more than 4 weeks could cause some moderate side effects, especially rashes or some skin allergy. This percent gradually increases with increasing dose administration especially for more than 2 months, as a percent and probability of experiencing side effects increases as well.

The eighth study: It demonstrated that *Echinacea purpurea* can be beneficial in increasing the immune response towards an antigen or infection to neutralize it (like to produce antibodies faster) such as virus infection, including the common cold, common influenza viruses, H5N1, H1N1, H2N1, SARS-CoV, and SARS-CoV-2. Also, higher doses of *Echinacea purpurea* can produce faster immune response than normal therapeutic doses, higher doses such as 700-1000mg three times daily or its active constituents via intravenous injection, give a better and more rapid response, especially in patients with serious or fatal disease infections, but the rash develops faster.

From all these studies, we can notice that there are some clear significant data, and there are some data that needed to be more clearer via conducting more studies with larger sample sizes. Despite the presence of many previous studies that have shown similar results about using immunostimulant herbs in the treatment and prophylaxis of some diseases such as common cold and influenza (31,32,33), but I failed to find studies have explored any information about immunostimulant substances (Especially *Echinacea purpurea*) and their uses in the treatment and prophylaxis of other influenza virus infections, including H5N1, H1N1, SARS-CoV, and SARS-CoV-2. However, new research should be conducted for clearer and significant results.

5. Conclusion

The study in this paper revealed that using of immunostimulant drugs such as *Echinacea purpurea* (with typical dose and recommended regimen therapy) can produce positive effects in treatment and prophylaxis of common cold.

Also, it has positive effects in the treatment and prophylaxis of influenza infections, including H5N1, H1N1, SARS-CoV, and SARS-CoV-2. Especially, if it combined with the usual drug treatment regimen and additive medications (especially multivitamins and minerals, such as Vitamins D, C, Zn mineral, hot drinks link ginger syrup or mint syrup, B2 receptor agonist such as salbutamol, and expectorant like guaifenesin).

Besides, it has positive effects on the prophylaxis of some other infectious diseases like upper and lower respiratory tract infections. Also, higher doses of it or its active constituents, through intravenous injection, can produce faster immune responses than typical therapeutic doses, but the rash could appear faster.

Some vaccinated people (people who are living in sunny hot weather, 27-35 degrees Celsius with Bacille Calmette-Guérin (BCG) showed some better results in the treatment of SARS-CoV-2.

Although many previous studies have shown similar results about using immunostimulant herbs in the treatment and prophylaxis of common cold and influenza, I did not find any study about using of immunostimulant substances in the treatment and prophylaxis of other influenza virus infections, including H5N1, H1N1, SARS-CoV, and SARS-CoV-2. However, other studies should be conducted for creating stronger evidences.

Availability of Data and Material: People and healthcare givers provided me the required information without any identification data which do not need any consent or any legal permission.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE:

Not applicable.

CONSENT FOR PUBLICATION:

Not applicable.

ACKNOWLEDGMENTS:

The author expresses a deep sense of acknowledges to everybody for helping in this research.

CONFLICT OF INTEREST AND FUNDING:

This research is funded by the author only, and no potential conflicts of interest exist.

References:

1. Kumar, S, Gupta P, Sharma S, Kumar D. "A review on immunostimulatory plants". *Journal of Chinese Integrative Medicine*. 2011; 9(2): 117-128.
2. Wira CR, Crane-Godreau M, Grant K. "Endocrine regulation of the mucosal immune system in the female reproductive tract". In Ogra PL, Mestecky J, Lamm ME, Strober W, McGhee JR, Bienenstock J (eds.). *Mucosal Immunology*. San Francisco: Elsevier. ISBN 0-12-491543-4. 2004.
3. Lang, TJ. "Estrogen as an immunomodulator". *Clin Immunol*. 2004;113(3): 224-230.
4. Dorshkind, K; Horseman ND. "The Roles of Prolactin, Growth Hormone, Insulin-Like Growth Factor-I, and Thyroid Hormones in Lymphocyte Development and Function: Insights from Genetic Models of Hormones and Hormone Receptor Deficiency". *Endocrine Reviews*. 2000;21(3): 292-312.
5. Nagpal, Sunil; Songqing Naand; Radhakrishnan Rathnachalam. "Noncalcemic Actions of Vitamin D Receptor Ligands". *Endocrine Reviews*. 2005; 26(5): 662–687.
6. Labh SN, Shakya SR. Application of immunostimulants as an alternative to vaccines for health management in aquaculture. *Int J Fish Aquat St*. 2014; 2 (1): 153-6.
7. Raman, Ram. Application of herbal-based immunostimulants in aquaculture: an overview. 2017.
8. N. Van Hai, The use of medicinal plants as immunostimulants in aquaculture: a review, *Aquaculture*. 2015;446(1): 88-96.
9. Ramalingum N, Mahomoodally MF. The therapeutic potential of medicinal foods. 1st ed *Adv Pharmacol Sci*. 2014.
10. Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. *Metabolites*. 2012;2(2):303-36.
11. Patil US, Jaydeokar AV, Bandawane DD. Immunomodulators: A pharmacological review. *Int J Pharm Pharm Sci*. 2012;4(1):30-6.
12. Dutt SB. PA02. 10. A review on immunomodulator activity of some indigenous medical plants. *Anc Sci Life*. 2013;32(2):2-55.
13. Salzberg, Steven L, Fraser, Claire M., Lipman, David J, Jill, *et al*. "Large-scale sequencing of human influenza reveals the dynamic nature of viral genome evolution". *Nature*. 2005;437(7062): 1162–1166.
14. Swine influenza. *The Merck Veterinary Manual*. 2008. ISBN 978-1-4421-6742-1. Archived from the

15. "ICTV Taxonomy history: Severe acute respiratory syndrome-related coronavirus" (html). International Committee on Taxonomy of Viruses (ICTV). Retrieved 2019-01-27.
16. "Naming the coronavirus disease (COVID-19) and the virus that causes it". World Health Organization (WHO). Archived from the original on 28 February 2020. Retrieved 28 February 2020.
17. Ian Brace. Questionnaire design: How to Plan, Structure and Write Survey Material for Effective Market Research. 2008;3:1-5.
18. M.N, Sarkies, K.-A, Bowles, E.H. Skinner, et al: Data Collection Methods in Health Services Research. Hospital Length of Stay and Discharge Destination, ACI Applied Clinical Informatics. Vol. 6, No. 1, 2015. pp. 96-109.
19. Biros M. Research without consent: Current status. *Ann Emerg Med.* 2003;42:550-64.
20. Biros M. Research without consent: Exception from and waiver of informed consent in resuscitation research. *Sci Eng Ethics.* 2007;13:361–9.
21. Matthew B. Weinger, Jason Slagle, Sonia Jain, *et al.*: Retrospective data collection and analytical techniques for patient safety studies, *Journal of Biomedical Informatics.* 2003;36:1-2.
22. Valen E. Johnson and col, Revised standards for statistical evidence', Proceedings of the National Academy of Sciences of the United States of America, November 11, 2013.
23. Weiss, D. J. Nominal analysis of “variable”. *Behavior Research Methods.* 2009; 41: 901-908.
24. Midgley JW. Southeastern Wildflowers: Your complete guide to plant communities, identification, and traditional uses. Crane Hill Publishers. ISBN 978-1-57587-106-6. 2005.
25. Manayi A, Vazirian M, Saeidnia S. "Echinacea purpurea: Pharmacology, phytochemistry and analysis methods". *Pharmacognosy Reviews.* 2015; 9 (17): 63-72.
26. "Echinacea". National Center for Complementary and Integrative Health. 2011-11-09.
27. Karsch-Völk M, Barrett B, Kiefer D, Bauer R, Ardjomand-Woelkart K, Linde K. "Echinacea for preventing and treating the common cold". *The Cochrane Database of Systematic Reviews (Systematic review).* 2004;2(2): CD000530.
28. Maton D, Hopkins J, McLaughlin CW, Johnson S, Warner MQ, LaHart D, Wright JD, Kulkarni DV. *Human Biology and Health.* Englewood Cliffs, New Jersey, US: Prentice Hall. ISBN 0-13-981176-

1.1997.

29. "Vital and Health Statistics Series. 11, No. 247 (03/2005)" (PDF). Retrieved 2 February 2014.
30. Cutolo, M; Sulli A; Capellino S; Villaggio B; Montagna P; Seriolo B; Straub RH. "Sex hormones influence on the immune system: basic and clinical aspects in autoimmunity". *Lupus*. 2004;13(9): 635-638.
31. Woelkart K, Linde K, Bauer. "Echinacea for preventing and treating the common cold". *Planta Medica*. 2008;74 (6): 633-7.
32. Schulten, Brigitte & Bulitta, Michael & Ballering-Brühl, Brigitta & Köster, Ulrike & Schäfer, Michael. (2001). Efficacy of Echinacea purpurea in patients with a common cold. A placebo-controlled, randomised, double-blind clinical trial. *Arzneimittel-Forschung*. 2001;51(10):563-8.
33. Shah SA, Sander S, White CM, Rinaldi M, Coleman CI. "Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis". *The Lancet. Infectious Diseases*.2007; 7(7): 473-80.
34. "BCG vaccines: WHO position paper ". *Weekly Epidemiological Record*. 2028;93(8): 73-96.
35. Neuzil KM, Maynard C, Griffin MR, Heagerty P. Winter respiratory viruses and health care use: a population-based study in the northwest United States. *Clin Infect Dis*. 2003;37:201-7.

Corresponding Author:

Sameh Monir Abdou Desouki*,

Clinical Pharmacy Specialist, Master in Clinical Pharmacy,

Clinical Pharmacy Specialist at Sameh Pharmacy, Egypt.

Former Pharmacist in Gizan General Hospital, KSA

Email: sammon2002@yahoo.com

<https://orcid.org/0000-0001-7003-5506>