



Research Article

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**PATIENT REPORTED OUTCOMES AND PATIENT SATISFACTION WITH HYPERISINCE®
(AN AYURVEDIC MEDICINE/POLY-HERBAL COMBINATION) IN HERPES SIMPLEX**

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ABSTRACT

Herpes simplex is a highly prevalent, self limiting viral infection. Complications, drug resistance and side-effects of anti-viral drugs make treatment of herpes simplex challenging. Herbal/Ayurvedic medicines have shown potential in herpes simplex management. We conducted a survey to know the patient reported outcomes of patented Ayurvedic formulation Hyperisince®. 122 herpes simplex infected patients who were treated with Hyperisince® were mailed a questionnaire containing 20 questions. The questions collected demographic information, disease information and patient feedback on Hyperisince®. A total of 101 responses were eligible for evaluation. HSV-1 was present in 31 patients, 48 had HSV-2 and 17 were infected with both the types. Eighty eight (87.13%) were previously treated with other drugs and acyclovir was the most common previous treatment. Symptom relief was reported by 76% of patients. Duration of herpes and nerve pain decreased considerably following Hyperisince® treatment. There was decrease in frequency of symptoms. The efficacy of Hyperisince® was more pronounced when it was used for >4 months. Twenty one patients rated Hyperisince® 10 out of maximum rating of 10 and 58 participants rated it ≥5. Hyperisince® was effective in relieving symptoms, nerve pain, and improving overall well being. Hyperisince® also reduced the likelihood of having another herpes outbreak, especially when taken for 4 months or more. Most patients rated efficacy as ≥5 in the scale of 10. Efficacy of Hyperisince® was more pronounced when used for >4 months. Further clinical trials can confirm our findings.

Key words: Herpes simplex, Hyperisince, herbal, Ayurveda

INTRODUCTION

Herpes simplex is a highly prevalent viral infection caused by either herpes simplex virus-1 (HSV-1) or HSV-2. While HSV-1 mostly affects oral area of the body, HSV-2 mostly affects genital area; though cross-over is also prevalent.¹ Among the two herpes simplex viruses, HSV-1 infection is more prevalent, affecting 3709 million people across the world (67%) belonging to the age group 15 – 49 years.² Whereas, HSV-2 is less prevalent than HSV-1 and it affects 417 million people (11.3%) world over.³

Herpes simplex is a recurrent self limiting viral infection. However, complications of HSV, like encephalitis, meningitis, neonatal infection and keratitis makes the disease burdensome. In addition, human immunodeficiency virus (HIV) is 3 times more common in HSV infected population.⁴ Anti-viral drugs are used for the purpose of treatment, as prophylaxis or as pre-emptive measures in herpes simplex. Acyclovir, famciclovir,

and valaciclovir are commonly used anti-viral drugs in HSV-1 and HSV-2. Cidofovir, foscarnet, ganciclovir and valganciclovir are less commonly used anti-viral drugs in HSV. Increasing anti-viral drug resistance and adverse effects of drugs pose challenges to treatment of herpes.⁵ Thus, there is a need for safer and more effective treatment options for herpes simplex.

Traditional medical practitioners have been using herbal medicines for management of diseases including infections. Plant extracts from *Hypericum mysoreense*, *Hypericum hookerianum* and *Usnea complanta* showed significant anti-viral efficacy in a study by Vijayan et al.⁶ We did a survey to evaluate patient satisfaction and patient reported (HSV infected) outcomes on efficacy and safety of herbal combination Hyperisince® (manufactured by Biogetica® see table 1 for ingredients; Hyperisince is licensed by Ayush as a Ayurvedic Treatment for Herpes and is marketed elsewhere as a herbal dietary supplement). Hyperisince® is GMP certified and manufactured at Deltas Pharma Pvt. Ltd. Uttarakhand.

Table 1: Ingredients of Hyperisince®

<p>Basant (<i>Hypericum mysoreense</i>) – 550 mg, Ashwagandha (<i>Withania somnifera</i>) roots -38mg, Bhumiamalaki (<i>Phyllanthus niruri</i>) – 38 mg, Chirabilva/Putikaranja (<i>Holoptelia integrifolia</i>) Bark – 28 mg, Khadira (<i>Acacia Catechu</i>) extracts of wood – 38 mg, Khus grass/ushir (<i>Vetiveria zizanioides</i>) – 28 mg, Lavanga (<i>Syzygium aromaticum</i>) - 38 mg, Haritaki (<i>Terminalia chebula</i>) Fruit - 38 mg, Nimba (<i>Azadirachta indica</i> Linn) Leaf extract - 38 mg, Yasthimadhu (<i>Glycyrrhiza glabra</i>) roots - 95 mg Liquorice root, Neerbramhi (<i>Bacopa monnieri</i>) extracts - 20mg, Kalmegh (<i>Andrographis paniculata</i>) – 30 mgs.</p>
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MATERIAL AND METHODS

A questionnaire was designed with 20 questions. Questions were in 3 domains – 1st domain collected demographic information, 2nd domain collected disease information and 3rd domain collected patient feedback on Hyperisince® (see Appendix I).

The questionnaire was randomly mailed to people who were treated with Hyperisince® at our clinic (Vijay Kamat's clinic) over past 5 years. The answers were collected electronically, were tabulated and analyzed. The data was analyzed using descriptive statistics. Ethics committee approval was not taken as it was a patient outcome measure survey. The participants

were completely informed about the activity and resultant publication and consent was obtained by asking a question on willingness to participate and share the data (see Appendix I).

RESULTS

The questionnaire was randomly sent to 122 patients through e-mails. Out of the 122 responses, consent was refused by 5 participants, while 16 remaining responses were not suitable for analysis. Responses of one hundred and one people were available for analysis.

Demographic Details

Of the 101 participants, 37 were female and 64 were male; 40 participants were married and 61 were unmarried. Fifty one participants had relationship with single partners and 19 with multiple partners while 31 were single. The average age of the individuals who participated in the survey was 44.5 ± 11.66 years. Mean age at which participants' encountered herpes was 31.15 ± 10.47 years. Thirty six participants reported of being infected with HSV-1, 48 of HSV-2 and 17 were infected with both the types. Ninety four participants were non-reactive for HIV while 7 of them were reactive. Fifty participants reported the consumption of alcohol while 42 did not consume alcohol.

Disease Details

The most common site of the manifestation was genitalia, which was reported by 78 participants. Nine participants had oral manifestation whereas 13 had manifestation at both the sites. One participant did not answer the question.

Details of Past Treatment

Eighty eight (87.13%) participants had taken some or the other kind of therapies [allopathic medicines (n=18), homeopathy medicines + herbal medicines + nutrition supplements (n=16), Over the counter medicines (OTC) (n=16), allopathic medicines + herbal medicines + OTC (n=10) and not specified responses (n=14)]. There were 27 participants who had tried all possible treatment options. Thirteen participants did not take any treatment in the past. Fifty seven participants did not report any allergy or intolerance to previous treatment, while those reported were mild conditions such as skin rash, headache, hair loss and so on. Acyclovir was the most prevalent treatment - 29 patients took acyclovir with no success and 25 patients took antivirals in conjunction with Hyperisince®.

Use of Tab. Hyperisince®

The duration of treatment of Hyperisince® varied from few days to years. Of the 101 participants, 69 had taken Tab. Hyperisince® in combination with other therapies, while 28 participants had taken Hyperisince® alone. Four participants had used Hyperisince® both in combination and alone for some period of time. Sixty four patients had used other supplements like Monolaurin®, Herpes Nosode® and Regimmune®. There was no difference in the results of the patients who took Hyperisince® alone or in combination with other remedies.

Patient Reported Outcomes of Efficacy of Hyperisince®

The efficacy of Tab. Hyperisince® was assessed based on following parameters – frequency of outbreaks, average duration of episodes and nerve pain before and after consumption of Tab. Hyperisince®; symptom relief following treatment with Hyperisince®. Out of 101 patients, 1 did not answer on frequency of symptoms, 1 patient did no answer on duration of episodes and 15 patients did not answer question on nerve pain. Among 101 patients, 76% patients experienced symptom relief.

Table 2: Frequency of symptoms

Frequency	Before	After
Constant	18	05
Twice a month	16	07
Monthly	21	28
Once a year	02	10
Twice a year	07	08
3 to 6 times/year	30	27
No outbreak in ≥ 2 years	06	15
Unanswered	01	00
None	00	01

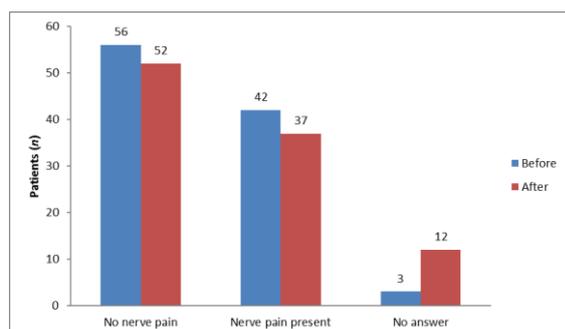


Figure 1: Nerve pain before and after treatment with Hyperisince

Table 3: Average duration of episodes

Duration of episodes	Before	After
1 day	02	14
1 to 3 days	00	02
3 days	10	31
3 days to 1 week	03	03
1 week	46	30
2 weeks	26	01
1 to 2 weeks	00	09
2-3 weeks	01	00
1 month	13	10
Unanswered	00	01

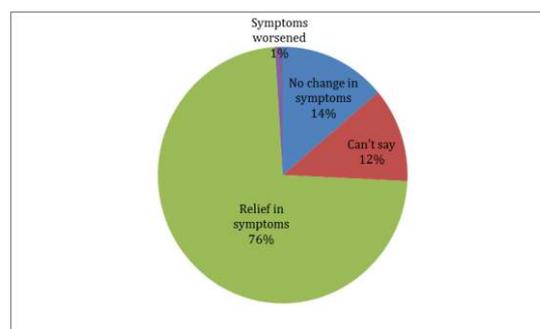


Figure 2: Status of symptoms

There was an overall reduction in frequency of outbreaks and symptoms after treatment with Tab. Hyperisince® (Table 2). While 18 patients had constant symptoms before treatment and only 5 had constant symptoms after treatment with Hyperisince®. Similarly, more number of patients (n=15) had no outbreaks for ≥2 years following Hyperisince® treatment vs. before treatment (n=6). The duration of herpes episodes considerably decreased after Tab. Hyperisince® treatment (Table 3). There was considerable decrease in the nerve pain following Hyperisince® treatment (Figure 1).

The participants were asked about the effect of Hyperisince® on the status of their symptoms. Out of 101 patients, 76% respondents reported relief in symptoms, while 12% were not sure of change in symptoms, 14% observed no change in symptoms. Only 1% of participants reported increase in symptoms (Figure 2).

Improvements in condition were seen in higher percentages for patients who took Hyperisince® for a period ≥4 months. Out of the patients who took Hyperisince® for ≥4 months, 50% were completely free of symptoms, 36% were somewhat better, 4% couldn't say if they were better and 10% had no change in symptoms. Forty five participants reported additional benefits like lower stress, energetic feeling and overall better health with use of Hyperisince®. It was observed that treating patients with Hyperisince® for ≥4 months decreased the future possibility of outbreaks.

In the patients who took past acyclovir treatment, taking Hyperisince® marginally improved frequency of outbreaks and duration of outbreaks. Patients taking Hyperisince® had lower frequency of outbreaks and shorter duration of outbreaks when compared to acyclovir treated patients (Table 4). While 24.14% of patients taking acyclovir had at least 2 outbreaks a month, only 3.44% of patients treated with Hyperisince® had 2 outbreaks a month.

Table 4: Frequency and duration of outbreaks during current Hyperisince® treatment and past acyclovir treatment

Frequency of outbreaks				
Frequency	Acyclovir		Hyperisince®	
	n	%	n	%
2 times/yr	1	3.44	2	6.89
3 times/yr	1	3.44	4	13.79
4 times/yr	7	24.14	5	17.24
6 times/yr	5	17.24	2	6.89
Constant	1	3.44	--	--
Monthly	5	17.24	9	31.03
Once/2 yr	2	6.89	1	3.44
2 times/month	7	24.14	1	3.44
Once a year	--	--	1	3.44
No outbreaks over 3 years	--	--	4	13.79
Duration of outbreaks				
1 day	1	3.44	4	13.79
3 days	3	10.34	7	24.14
1 week	14	48.27	10	34.48
2 weeks	6	20.68	3	10.34
1 month	5	17.24	5	17.24

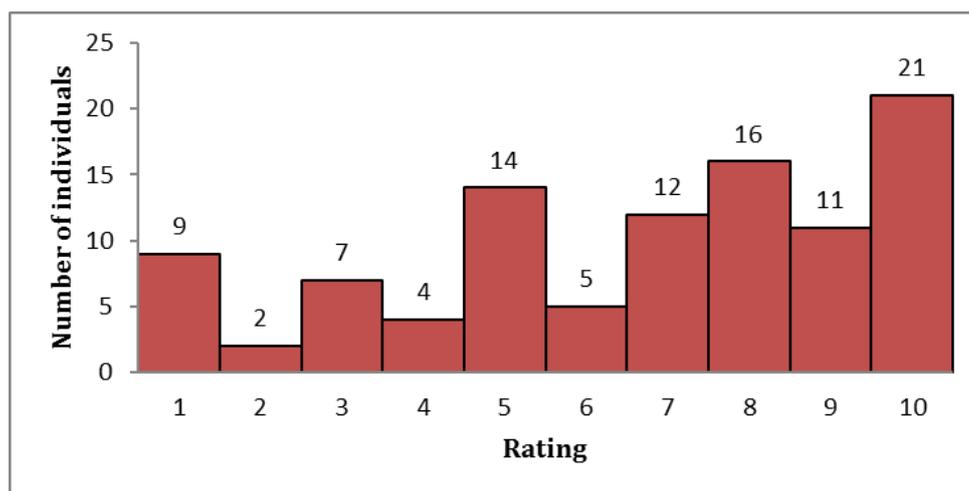


Figure 3: Patient rating of Hyperisince® out of a maximum rating of 10

Patient Rating of Hyperisince® in Herpes simplex

The participants were also asked to rate the formulation on a scale of 1 to 10 (1 being the lowest and 10 being the highest). The mean rating score for the formulation was found to be 6.64 ±2.86. Twenty one participants scored Hyperisince® 10 on the

scale of 10; 58 scored ≥5 on the scale of 10 and 36 rated it ≤5 (Figure 3). Overall, the patient rating for Hyperisince® was high.

DISCUSSION

The present study was carried out to study the usefulness of Ayurvedic Medicine Tab. Hyperisince® for oral and genital herpes. It was found that the frequency of outbreaks was reduced after treatment with Tab. Hyperisince®. The duration of episodes was considerably reduced along with a marked reduction in nerve pain. There were no evident adverse events observed.

Tab. Hyperisince® is a polyherbal patented dietary supplement with the chief constituent *Hypericum mysorense*. Reported studies show that methanol extracts of the aerial parts of *Hypericum mysorense* and *Hypericum hookerianum*, have exhibited detectable antiviral effect in HSV-1 with an inhibitory concentration for 50% (IC₅₀) of 100 and 50µg/ml respectively. The extracts of *Hypericum mysorense* and *Hypericum hookerianum* exhibited virus inhibitory activity by both CPE inhibition assay and virus yield assay.⁷

Conventional antiviral drugs have proven effectiveness for genital herpes but it is noted that there is no evident antiviral drug that can alter the natural history of genital herpes in humans and curtail the recurrent nature of the disease. Therefore patients continue to use a variety of complementary and alternative medicine (CAM) treatments.^{8,9} Most patients in the study had used conventional anti-viral drugs in the past and most of them reported fewer outbreaks and shorter outbreaks when on Hyperisince® than when they were on acyclovir. Furthermore the adverse events and side effects were greatly reduced as well.

Various studies have been reported on the use of herbs in the management of Herpes. *Echinacea purpurea*, has shown activity against HSV-2. However the efficacy of oral therapy with a product containing an *Echinaceapurpurea* extract (95% plant/5% root), for the treatment of genital herpes failed to show a statistically significant benefits.¹⁰

In early in vitro studies, L-lysine has shown an inhibitory effect on HSV replication but failed to prevent virus reactivation in explanted ganglia. While several clinical studies have suggested that certain doses of L-lysine supplements are beneficial in reducing either the frequency of recurrences or time to healing, others did not find improved outcomes for one or both of those endpoints. Hence studies conducted to date do not provide sufficient information to address the use of L-lysine in patients with HSV infections.⁹

In the present study, we evaluated the responses of patients consuming the dietary supplement Tab. Hyperisince®. We observed that Tab. Hyperisince® decreased the frequency and average duration of episodes in patients suffering from herpes. It also decreases the post herpetic neuralgia, which is a complication of herpes. The participants rating about the

formulation indicated that the formulation is satisfactory. In short, Tab. Hyperisince® is found to be an effective as an herbal supplement and an Ayurvedic medicine to treat the symptoms of herpes and reduce the recurrence of outbreaks as reported by patients in this study.

Most patients had less outbreaks and it is promising to note that a considerable number of patients had no recurrence of herpes outbreaks for >2 years after taking tab Hyperisince®. Tab. Hyperisince® reduced the average duration of episodes to 1 to 3 days from 1 week to 1 month on an average.

Of the 101 respondents, 36 participants reported of being infected with HSV-1, 48 of HSV-2 and 17 were infected with both the types. It was also observed that the most common site of the manifestation was genitalia, which was reported by 78 participants. Nine participants had oral manifestation whereas 13 had manifestation at both the sites which is supportive of the shifting trend.

Initially HSV-1 was thought to be an infection of the mouth or lips, although in later decades it has been considered a cause of genital herpes as well. With the change in sexual practices such as increased oro-genital sex, it is likely that both HSV-1 and 2 would be common causes of initial infection as observed in our study.¹¹

Further, HSV infection is associated with a 2–4-fold increased risk of acquiring HIV infection.¹² However in our study it was observed that 97 out of the 101 respondents were non-reactive to HIV.

There were no evident adverse events noted after consumption of Tab. Hyperisince® as reported by the respondents of the study. On the contrary, 45% participants reported of some benefits in addition to relief in symptoms of herpes. The participants reported of feeling more energetic, lighter and healthier.

The study had several limitations. This questionnaire was not administered in person but electronically to patients who had used Hyperisince® in past. The data on diagnosis of herpes by herpes type is not clearly known as >50% of the patients did not report the diagnosis with type of virus. There may be lacunae in accuracy of outcome reported by patients as the subjective outcomes were not matched with clinical outcomes. The responses are subjective and objective evaluations of subjective responses were not done. The data was analysed using descriptive statistics.

A well planned clinical study with precise investigations can further establish the efficacy of Tab. Hyperisince® as an effective supplement in the management oral and genital herpes.

CONCLUSION

Tab. Hyperisince® was reported as effective by patients in terms of decreasing frequency of herpes simplex episodes, decreasing average duration of episodes, nerve pain and relieving symptoms. In addition, patients reported improvement of general health. The benefits of Hyperisince® were even greater for participants who took Hyperisince® for 4 months or more. Further well-designed clinical trials would be helpful in understanding efficacy and safety of herbal combination Hyperisince® in herpes simplex infections.

Appendix A. Questionnaire

Domain I: Demographic Data

1. Do you agree to participate in this Study?
 - Yes
 - No
2. Name:
3. Sex:
 - Male
 - Female
4. Age:
5. Marital Status
 - Married
 - Unmarried
6. Please mention your relationship status
 - Relationship with single partner
 - Relationship with multiple partners
 - Single
7. Do you consume alcohol?
 - Yes
 - NoIf yes please specify the units per week:
8. Have you taken any treatment in the PAST for this condition?
 - Yes
 - No

If YES please specify

- Allopathy/ Conventional medicine
 - Homeopathy
 - Herbals
 - Nutraceuticals/ Nutritional supplements
 - Over the counter treatment
 - Diet
 - Yoga/Pranayama/ Meditation/Reiki/Other stress reduction regimen
 - No treatment
 - Other
9. How long did you take Hyperisince®:
 10. Have you tried Tab .Hyperisince® alone or in combination with other therapies?
 - Alone
 - CombinationIf in COMBINATION, in combination with what?
 - Prescription drugs (Allopathy/conventional medicine)
 - Homeopathy
 - Herbals
 - Nutraceuticals/Nutritional supplement
 - Over-the-counter treatment
 - Yoga/Pranayama/Meditation/Reiki /other stress reduction regimen
 - Local applications such as Visarpa clay

Domain II: Details of Disease and Severity

11. Do you know what type of herpes do you have? If yes, is it?
 - HSV-1
 - HSV-2

12. Have you been diagnosed as HIV +ve?
 - Yes
 - No
13. What is the site of manifestation of symptoms?
 - Oral
 - Genital
14. Please mention the frequency of outbreak recurrences before taking Tab. Hyperisince®
 - Constant
 - Twice a month
 - Monthly
 - 6 times a year
 - 4 times a year
 - 3 times a year
 - 2 times a year
 - Once a year
 - Once in two years
 - Once in three years
 - No outbreak for three or more years
 - Other
15. Please specify the average duration of outbreak before taking Tab. Hyperisince®
 - 1 day
 - 3 days
 - 1 week
 - 2 weeks
 - 1 month

Domain III: Effects of Hyperisince®

16. What was the status of your symptoms after taking Tab. Hyperisince®?
 - All symptoms relieved
 - Somewhat better
 - No change in symptoms
 - Symptoms worsened
 - Can't say
17. Please mention the frequency of outbreak recurrences after taking Tab. Hyperisince®
 - Constant
 - Twice a month
 - Monthly
 - 6 times a year
 - 4 times a year
 - 3 times a year
 - 2 times a year
 - Once a year
 - Once in two years
 - Once in three years
 - No outbreak for three or more years
 - Other
18. Please specify the average duration of outbreak after taking Tab. Hyperisince®
 - 1 day
 - 3 days
 - 1 week
 - 2 weeks
 - 1 month
19. Have you noticed a reduction in pain after taking Hyperisince®?
 - Yes
 - No
20. How do you rate the overall effectiveness of Hyperisince® on a scale of 1 to 10?
1 2 3 4 5 6 7 8 9 10

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