

## Clinical Researches

Clinical Evaluation of *Shilajatu Rasayana* in patients with HIV Infection

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## Abstract

AIDS is one of the serious global health concerns caused by Human Immuno Deficiency(HIV) virus and is predominantly a sexually transmitted disease. Currently there is no vaccine or cure for AIDS still Anti Retroviral Therapy (ART) is successful. It reduces both the mortality and the morbidity of HIV infection, but is expensive and inaccessible in many countries. However intense the therapy may be, HIV virus is rarely eliminated, and drug resistance is a major setback during long-term therapy. The development of new drugs and strategies and exploring alternative systems of medicine for antiviral herbs or drugs is the need of the age to improve treatment outcomes. *Ayurveda* describes many diseases which incorporate HIV like illness e.g. *Rajayakshma*, *Ojo Kshaya*, *Sannipata jwara* etc. HIV infection affects multisystems, chiefly the Immune System which can be correlated to *Ojo Kshaya*. *Rasayana Chikitsa* is the frontline therapy employed to treat *Ojus* disorders. Therefore *Shilajatu* (Mineral pitch), *Centella asiatica* (*Mandukaparni*), *Tinospora cordifolia* (*Guduchi*) and *Embllica officinalis* (*Amalaki*), well known for their Immuno-modulator and antioxidant properties were selected to evaluate their role on immune system. The study was carried on 20 patients from OPD and IPD of *Kayachikitsa*, S.S.Hospital, IMS, BHU and was randomly allocated into Treated group (*Shilajatu*+ART) and Control group (ART). Treated Group responded better to ART both clinically and biochemically. The results show that *Shilajatu* decreases the recurrent resistance of HIV virus to ART and improves the outcome of the therapy

**Key words:** HIV Virus, AIDS, ART, *Rasayana*, *Shilajatu* and CD<sub>4</sub> count.

## Introduction

AIDS is one of the major global health concerns, highly infectious, and stands first as a sexually transmitted and incurable disease. AIDS is now a pandemic and globally, an estimate of 33 million people are affected with AIDS and AIDS has killed an estimate of 2.1 million people in 2007. Over three-quarters of these deaths occurred in sub-SAHaran Africa, retarding economic growth and destroying human capital<sup>1</sup>.

AIDS is caused by Human Immuno Deficiency virus (HIV). HIV is a retrovirus that primarily targets CD<sub>4</sub><sup>+</sup> helper T (a subset of T cells), cells that are responsible for the Immunity of an individual. Once HIV has killed so many CD<sub>4</sub><sup>+</sup> T cells and there are fewer than 200 of these cells per microliter (μL) of blood, cellular immunity is lost

and the person has said to be suffering from AIDS. This infection progressively reduces the effectiveness of the immune system and leaves individuals easily susceptible to opportunistic infections and tumors. HIV is transmitted through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV, such as blood, semen, vaginal fluid, seminal fluid, and breast milk. This transmission can involve anal, vaginal or oral sex, blood transfusion, contaminated hypodermic needles, exchange between mother and baby during pregnancy, childbirth, breastfeeding or other exposure to one of the above bodily fluids<sup>2</sup>.

As per (UNAIDS definition)<sup>3</sup>. ABC of AIDS prevention are:

- A- Abstinence or delaying first sex.
- B- Being safer by being faithful to one partner or by reducing the number of sexual partners.
- C- Correct and consistent use of condoms for sexually active young people, couples in which one partner is HIV-positive<sup>3</sup>.

Currently there is no vaccine or cure for AIDS. Anti Retroviral Therapy (ART) is successful. It reduces both

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the mortality and the morbidity of HIV infection, but is expensive and inaccessible in many countries.

Clinical picture of AIDS, described in *Ayurveda* is found scattered in all authentic texts. Immunity has been explained under the concept of *Ojus*. Clinical features of *Ojus*, its formation, features of derangement-*Visramsa*, *Vyapat* and *Kshaya*<sup>4,5</sup> are explained in detail by the authors like *Charaka*, *Sushruta* and *Vagbhata* in their texts. Stages of AIDS resemble *Hatoujas* a complicated type of fever, *Ojanirodhaka Jvara*, *Shosha*, *Madhumeha*, *Asadhya Pandu*, *Rajayakshma* and *Udanavrata Prana Vata* in *Ayurveda*. Here AIDS and its opportunistic infections have been correlated with *Ojo Kshaya*. The virus invades the *Rasadi sapta dhatus* and causes decrement in their quality and quantity. In *Ayurveda*, *Ojus* is the essential substance of all *dhatus* and determines the capacity of the individual to combat the disease (*Vyadhibala virodhitvam*) and the power to resist the virulence of disease (*Vyadhi utpadaka pratibandhakatvam*) causing factors in future<sup>6</sup>.

For the process of rejuvenation, *Ayurveda* has described a unique therapy-*Rasayana* therapy. Drugs described under *Rasayana* act on *Agni*, *Dhatu* and *Srotas* level and help in formation of *prashasta dhatus* maintaining a perfect equilibrium of all the *doshas* and *dhatus*. *Shilajatu* is one of the best of the *rasayanas* described by *Charaka*, *Sushruta* in all diseases where *Bala* i.e *Ojus* is involved. Hence *Shilajatu* along with *Mandukaparni*, *Guduchi* and *Amalaki*, well known *rasayana* herbs were selected to evaluate their role in boosting the immunity.

## Aims and Objectives

1. To study the concept of *Ojus* in HIV Infection/AIDS in *Ayurveda*.
2. To study the effect of *Shilajatu* (Mineral pitch) in HIV positive cases associated with opportunistic infection receiving ART.
3. To study the probable mode of action *Shilajatu* treated with *Centella asiatica*, *Tinospora cordifolia* and *Emblica officinalis* in the patients of HIV.
4. To study the short term safety profile of *Shilajatu Rasayana* in the patients of HIV.

## Material & Methods

A total of 20 diagnosed cases of HIV infection receiving ART were selected from the OPD and IPD of *Kayachikitsa*, S.S.Hospital, IMS, BHU, after thorough examination and obtaining informed consent.

### Inclusion criteria

- Newly diagnosed cases.
- Patient not having many complications or many secondary infections.

- Patient of 20-50 yr. age group.
- CD<sub>4</sub> count not less than 150/ micro liter.
- Patients willing to participate and giving informed consent.

### Exclusion criteria

- Patients below 20 yr. and above 40 yr. age group.
- Patients having multiple opportunistic infections and with complications like Diabetes, HTN, *Asthma* etc.
- Pregnant and lactating women.

### Diagnostic criteria

1. History taking like profession, having sex with many partners, blood transfusion etc.
2. Presence of clinical sign and symptoms suggestive of HIV.
3. Biochemical investigations like ELISA for HIV I/II and CD<sub>4</sub> count.

### Study Design

This was a randomized, controlled clinical trial conducted in Dept.of *Kayachikitsa* after obtaining permission from the Institutional Ethical Review Committee of IMS, BHU.

The 20 selected and diagnosed cases of HIV infection were randomly allocated into two groups. The selected patients have undergone complete general examination to rule out any gross abnormalities and were evaluated clinically and biochemically to confirm the diagnosis.

### Grouping

**Control Group (Gr-B) (N=8):** Patients were given HAART Therapy from the AIDS clinic of Modern Medicine, S.S.Hospital, IMS, BHU.

**Treated Group (Gr-A) (N=12):** Patients were given ART along with *Shilajatu Rasayana* for 3 months.

**Form of the trial drug:** Capsules of 500mg each.

**Route of Administration:** Oral

**Duration:** 3 months.

### Selection of drug:

*Shilajatu Rasayana* was selected as a trial drug in the treatment of HIV positive patient. *Shilajatu* had been explained a very popular drug for *Oja Kshaya* in case of *Madhumeha* by *Charaka* in *Chikitsasthana*, chapter 1/364-367, and *Sushruta* in *Chikitsa sthana* 13/16.

**Dose:** *Shilajatu Rasayana* was used for 3 months in two methods.

1. **Kalpa Prayoga:** *Shilajatu* capsules was used for 15 days. Starting with 1gm and increasing 2 gm on every day for 5 days unto 9g. (1 gm, 3 gm, 5 gm, 7 gm, 9 gm,); 9 grams was continued for further 5 days

and finally decreased in the similar fashion, 2 gms. every day for 5 days up to 1 gm.

2. *Continued Prayoga*: After 15 days of *Kalpa* therapy, a single dose of 6 gram per day was given up to 3 months of trial period.

### Preparation of Shilajatu Rasayana

The trial drug was prepared in the the Dept.of Rasa Shastra, IMS, BHU. *Shilajatu* was first purified with *Gomutra* for 7 times and then powdered. The powder was triturated with *Swarasa* of *Amalaki*, *Guduchi* and *Mandukaparni* 7 times each, and packed into 500mg capsules and stored.

*Follow-up and Assessment*: The initial two follow-up were done at an interval of 15 days in a month. Then other two follow-ups were done in 1 month. Efficacy of trial drug was assessed by (I) Relief in symptoms on a point rating score. (II) Changes in Biochemical investigation. Response was graded as follow:

1. *Improved*: The patient were getting better change in clinical sign and symptom, changes in biochemical reports (LFT, Renal profile) and gradual increase in value of CD<sub>4</sub>.
2. *Unchanged*: There is no improvement in the clinical feature and CD<sub>4</sub> count.

### Symptoms grading

#### 1. Depression:

- Absent - 0 - Normal behaviour
- Mild - 1 - Recurrently disturbed
- Moderate - 2 - Difficult to do job work
- Severe - 3 - Unable to work any job

#### 2. Weight loss

- Absent - 0 - No change in wt or increase in wt.
- Mild - 1 - Wt. loss <3 kg in 1month
- Moderate - 2 - Wt. loss 4-8 kg in 1 month
- Severe - 3 - Wt. loss >8 kg in 1 month

#### 3. Diarrhoea

- Absent - 0 - Stool 1-2 time/day with normal Consistency
- Mild - 1 - Stool 3-5 time/day
- Moderate - 2 - Stool 6-8 time/day
- Severe - 3 - Stool >8 time/day or passes of stools or on in take of any diet

#### 4. Fever

- Mild - 98.6°F - < 100°F
- Moderate - > 100°F- <102°F
- Severe - > 102°F

#### 5. Oral Thrush

- Absent - 0 - No foul smelling
- Mild - 1 - Occasional foul smelling
- Moderate - 2 - Continuous foul smelling
- Severe - 3 - Foul smelling with stomatitis

#### 6. Nausea/Vomiting

- Absent - 0 - No nausea & vomiting
- Mild - 1 - Occasional feeling
- Moderate - 2 - Feeling after intake of meal
- Severe - 3 - Recurrently vomiting habit

#### 7. Loss of Appetite

- Absent - 0 - Normal appetite
- Mild - 1 - Unable to take evening meal
- Moderate - 2 - Unable to take Solid meal
- Severe - 3 - Vomiting just after intake of meal

#### 8. Anaemia (Hb%)

- Absent - 0 - >14mg/dl in male  
>12mg/dl in female
- Mild - 1 - <14mg/dl - >12mg/dl in male  
<12mg/dl - >10mg/dl in female
- Moderate - 2 - <12mg/dl - >10mg/dl in male  
<10mg/dl - >8mg/dl in female
- Severe - 3 - <10mg/dl in male  
<8mg/dl in male

## Observation & Results

**Table 1: Effect of Shilajatu Rasayana on Various Symptoms:**

S. No	Symptoms	Control		Treated		t value	p value (<0.05)
		Mean ± S.D	Mean ± S.D	Mean ± S.D	Mean ± S.D		
		BT	AT	BT	AT		
1	Loss of Appetite	2.5±0.54	1.83±0.75	2.00±0.56	0.00±0.00	11.76	HS
2	Nausea/Vomiting	2.16±0.00	0.16±0.40	1.62±0.51	0.00±0.00	9.70	HS
3	Anemia	0.66±1.03	0.00±0.00	0.80±0.90	0.06±0.00	2.44	S
4	Weight Loss	2.16±0.25	0.33±0.51	2.30±0.67	0.00±0.00	11.6	HS
5	Diarrhoea	2.30±0.51	0.50±0.54	2.30±0.67	0.50±0.22	6.33	HS
6	Depression	2.50±0.54	0.83±0.15	2.00±0.94	1.00±0.81	7.74	HS
7	Fever	2.30±0.57	0.33±0.45	2.10±0.73	0.40±0.69	8.57	HS
8	Oral Thrush	2.10±0.40	1.16±0.75	2.10±0.56	0.5±0.70	6.79	HS
9	Pul.Tuberculosis	0.60±0.80	0.00±0.00	1.00±0.94	0.00±0.00	3.67	HS

**Table 2: Effect of Shilajatu Rasayana on biochemical parameters:**

S. No.	Biochemical Parameter	Control		Treated		t value	p value
		Mean $\pm$ S.D	Mean $\pm$ S.D	Mean $\pm$ S.D	Mean $\pm$ S.D		
		BT	AT	BT	AT		
1	CD <sub>4</sub> Count	170 $\pm$ 40.9	247 $\pm$ 28.3	164. $\pm$ 33.1	253 $\pm$ 31.	-31.34	<0.001HS
2	SGOT ( )	40.8 $\pm$ 5.26	45 $\pm$ 11.7	31.0 $\pm$ 4.65	24.3 $\pm$ 5.1	12.10	<0.001HS
3	SGPT ( )	37.66 $\pm$ 2.2	47.8 $\pm$ 11.6	36.3 $\pm$ 4.1	292 $\pm$ 5.61	8.10	<0.001HS
4	Alk.Ph ( )	230.3 $\pm$ 5.1	335 $\pm$ 76.1	195 $\pm$ 16.9	131.4 $\pm$ 6.9	11.14	<0.001HS
5	Urea ( )	29.33 $\pm$ 4.0	50.33 $\pm$ 4.4	29.3 $\pm$ 5.3	22.4 $\pm$ 2.0	5.85	<0.001HS

## 9. Tuberculosis

- Absent - 0 - No feature of tuberculosis  
 Mild - 1 - One system involvement  
 Moderate - 2 - More than 2 system involvement  
 Severe - 3 - Multiple system involve or miliary or MDR tuberculosis.

## Discussion

Total 20 patients HIV cases with various symptoms were enrolled in the trial. On randomization, 12 were kept on ART+Shilajatu Rasayana (treated group) while 8 patients received only HAART therapy. Two patients in each group were dropped out as they discontinued the trial drug without the permission of the investigator. Confirmation of HIV was done only by ELISA for HIV I and II. The history taking showed that out of 20 registered cases, 18 were males with Vata-Pittaj prakriti, aged between 31-40 years, belonging to labour class (drivers and coolies) all married and majority with multiple sex partner history.

Shilajatu (Mineral pitch) is a herbo mineral compound with many beneficial therapeutic properties<sup>8</sup>. It has been extensively used by all the Ayurvedic scholars in all chronic debilitating disorders since decades. It has Kashaya Tikta rasas, Sheeta virya, TridoshAhara, Vrishya, Balya, Mutrala, Lekhana, Yogavahi and Rasayana properties<sup>5</sup>. It has many rich, bioactive molecules (nutrients, iron manganese, phenols etc)acts a powerful adaptogen in the wear and tear phenomenon of aging process<sup>8</sup>.

Amalaki<sup>7</sup> and Guduchi<sup>7</sup>, share common properties. Amalaki is best among Vayasthpaka herbs. Amalaki, is fortified with Vit-C which is a natural, abundantly available powerful antioxidant, anti inflammatory and free radical scavenger of the metabolism<sup>9</sup>.

Guduchi among all Rasayanas. They possess TridoshAhara, Sheeta Virya, Dahaprashamana, Chakshushya, Keshya, Vayasthapaka, Hridhya, Rasayana, Vrishya, Pramehaghna, Yakriduttejak properties. Guduchi (Giloy) a bitter active principle has anti-inflammatory and hepato-protective properties. It acts on liver, the chief site of metabolism of food and drugs, normalizing the elevated transaminases and repletes the hepatocyte glutathione sod dismutases responsible for scavenging of free radicals<sup>11</sup>.

Mandukaparni possesses Tikta, Kashaya rasas, Sheeta Virya and Madhura vipaka and best among Medhya rasayanas. Fresh leaf extract has shown nootropic, tranquilising, memory enhancing, and adaptogenic properties on experimental models<sup>7,10</sup>.

All the above drugs act as immune-boosters and adaptogenic, which act both on the body and the mind improve physical strength of the individual to fight against opportunistic infections and allergies and correct the mood disturbances in AIDS.

Drug was prepared in Department of Rasa Shastra, IMS, B.H.U. Shilajatu was triturated seven times with the swarasas (fresh juice extracts) of all the three herbs separately for 7 days each dried, powdered and then filled in 500mg capsules. It was administered as mentioned in the material and methods for 3 months. Response was assessed on the basis of improvement in signs and symptoms and CD<sub>4</sub> count. Safety profile of the drug was assessed by its impact on Liver enzymes and Urea, Creatinine which were evaluated before and after trial.

Symptoms and signs were graded as 0-3 depending on the severity. After completion of trial period, observations are shown in Table1.

Treated Group (HAART+Shilajatu Rasayana) showed 100% improvement in loss of appetite, nausea and vomiting and depression, 80% in diarrhoea and weight loss, 60% in fever, anaemia and cough, 50% in the oral thrush and sore throat. The control showed only 70% improvement in anemia, fever, diarrhoea and weight loss; 50% improvement in loss of appetite, nausea, cough and depression.

Objective improvement was assessed by the increase in CD<sub>4</sub> count.Both groups responded more or less similarly but the control group showed rising values of SGOT, SGPT, Alkaline Phosphatase, Urea and Creatinine. The HAART is associated with hepatic and kidney decompensation which was successfully overcome by giving Shilajatu rasayana. Shilajatu, Amalaki and Guduchi by virtue of its properties enhances the immunity by increasing CD<sub>4</sub> T helper cell counts, prevents the resistance of HIV virus to ART drugs. It also enhances the excretion of Virus load from the body but needs to be substantiated by the data. AIDS has social stigma

and individuals with AIDS are socially boycotted and subjected to frequent insult, which makes their lives lead burdensome and frustrated. *Mandukaparni* is a *Medhya* herb with tranquilizing properties successfully improved the overall outcome of the trial drug.

*Shilajatu* has many rich, bioactive molecules (nutrients, iron manganese, phenols etc) acts a powerful adaptogen in the wear and tear phenomenon of aging process. *Shilajatu Rasayana* on triturating with *Amalaki*, is fortified with Vit-C which is a powerful antioxidant, *Guduchi* (Giloy) a bitter active principle has anti-inflammatory and hepato-protective properties. It acts on liver, the chief site of metabolism of food and drugs, improving its functions. ART is chiefly associated with alteration in Liver Function Tests, these were reversed and normalized by *Guduchi*. *Mandukaparni* fresh leaf extract has memory enhancing and tranquilising properties which treat the depression often associated with HIV patients.

## Conclusion

The compound formulation was found to be safe, (on prolonged use for 3 months in the dose of 6 gm ) and it has decreased the intensity of the clinical symptoms and signs and also protected the liver from the hepatotoxicity of ART as evident by normal LFT or Kidney function tests.

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## हिन्दी सारांश

### एड्स (एच.आइ.वी. इन्फेक्शन) रूग्णों में शिलाजतु रसायन का चिकित्सकीय प्रभाव

जी. डी. गुप्ता, एन. सुजाथा, अजय धनीक एवं एन. पी. राय

आयुर्वेद में राजयक्ष्मा, ओजक्षय, सन्निपात ज्वर जैसे संदर्भित लक्षण समुच्चय एड्स व्याधि के लक्षणों के साथ साधर्म्य रखते हैं। प्रस्तुत अध्ययन में इस व्याधि पर गुडूची, आमलकी एवं मण्डूकपर्णी स्वरस से भावित शिलाजीत रसायन का प्रभाव आधुनिक एण्टी रेट्रोवायरल थेरापी की तुलना में देखा गया। परिणाम स्वरूप शिलाजतु रसायन से लाक्षणिक तथा जैवरासायनिक परीक्षणों पर अधिक उत्साहवर्धक लाभ पाया गया।