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PIPPALI VARDHAMANA RASAYANA IS A SAFE AND EFFECTIVE ADJUVANT TO DOTS IN TREATMENT OF PULMONARY TUBERCULOSIS

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ABSRACT

Tuberculosis (TB) is an ancient scourge caused by *Mycobacterium tuberculosis* which may have originated about 20,000 – 15,000 years ago[1]. Of the estimated 9 million people who developed TB in 2013, more than half (56%) were in the South-East Asia and Western Pacific Regions. India alone accounted for 24% of global stages[2]. The trial was conducted to establish the efficacy of the *'VardhamānaPippalīRasāyana'* as an adjuvant therapy in the management of newly diagnosed cases of the Pulmonary Tuberculosis. The patients recruited were divided in two groups Group1 received DOTS regimen As recommended in RNTCP program (2 HREZ+4 HR) in supervision of DOTS (worker on alternate days of week).Group 2 received DOTS regimen As recommended in RNTCP program (2 HREZ/4 HR) in supervision of DOTS worker on alternate days of week along with ***'Vardhamāna Pippalī Rasāyana'*** **.** The patients who received DOTS treatment along with ***'Vardhamāna Pippalī Rasāyana'*** exhibited significant improvement in AFB reversibility, Weight gain, Hemoglobin (Hb%) and normalization of ESR. So DOTS treatment along with ***'Vardhamāna Pippalī Rasāyana'*** is a promising treatment strategy for management of Pulmonary tubesrculosis.

Keywords: *Vardhmāna PippaliRasayana, DOTS, TB*

INTRODUCTION

Tuberculosis (TB) is an ancient scourge caused by *Mycobacterium tuberculosis* which may have originated about 20,000 – 15,000 years ago[1]. Of the estimated 9 million people who developed TB in 2013, more than half (56%) were in the South-East Asia and Western Pacific Regions. India alone accounted for 24% of global stages[2].Every year 1.8 million persons develop TB, of which about 80,000 are infectious and until recently 37,000 died of it annually -1,000 every day. The disease is a major barrier to social and economic development. An estimated 100 million work days are lost due to illness.[3]The development of active tuberculosis is a function of the quantity and virulence of the invading organism and the relative resistance or susceptibility of the host to the pathogen. The risk of developing disease after being infected depends largely on endogenous factors, such as the individual's innate susceptibility to disease and level of function of cell-mediated immunity. The most frequent symptoms of pulmonary tuberculosis are cough, moderate to high grade evening rise fever, night sweats, weight loss and malaise.

Its description is available right from period of the *Ṛgaveda* (7000BC) *'Atharvaveda*&*Śuklayajurveda*(10,000BC). Its importance is evident from the fact that it has been included in one of eight prime diseases described by *ĀcāryaAgniveśa* in *CarakSaṁhitānidānasthāna*(section of etiologies and diagnosis)by name of *Śoṣa*and by name of *Rājyakṣma*in *cikitsāsthana*(Section of treatment strategies). It has been described by *Agniveśa* as one of the eight diseases that are difficult to cure and ultimately may lead to death even in their mildest form. *ĀcāryaSuśruta* has described it as one of infectious diseases in *Sūtrasthāna*. *ĀcaryaVāgbhatta* has notified it as disease which is notorious to destroy potency and efficacy of drugs.

Although effective combination chemotherapy for TB has been available for almost half a century but it has done little to reduce burden of the disease in low income countries including India. The prevalence, incidence and annual risk of the infection continues to be same as they were at time of baseline National survey fifty years ago. The number of the patients with active disease has continued to increase in proportion to growth of the population in India.

Problem with DOTS which comprises two months of treatment with 4 drugs (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol) followed by four months of 2 drugs (Rifampicin and Isoniazid) is the six months long duration of treatment itself. It is during this lengthy period that patient starts feeling well and therefore often stops taking treatment as a result there is relapse and emergence of drug resistance. It implies that, we are at the end of the era when some thirty years effective multidrug regimens have been available to cure almost all the cases however severe be the disease.

So there is an urgent need of newer, widely available, cost effective, palatable and safe drugs that have potential to shorten standard six months regimen with conventional drugs (2EHRZ/4RH). Such drugs would significantly reduce efforts required by TB control program.

Fruits of *Pippalī (Piper longum*Linn*)* are known to alleviate cough *(Kāsa)*, fever*(Jvara)*, dyspnoea*(Śvāsa)*& anorexia*(Aruci)* which are the cardinal diagnostic features of Pulmonary TB. It is known to pacify vitiated *Vāta&Kapha*which are primary elements in pathogenesis of *KṣayaRoga*. It promotes physical strength & libido by virtue of its *madhurvipāka*&*rasayana*(elixir)property. It is also known to exhibit antibacterial, anti-tubercular, imunostimulatory, anti-

inflammatory, anti-ulcerogenic and expectorant activity.

PippaīvardhamanRasāyana is special therapeutic regimen where patient is given 1000 (one thousand) *Pippalīs*over a span of approximate one month. The patient remains particularly on milk during this treatment regime. The regimen is started by giving five or ten *Pippalīs* in divided doses on day 1 and then increasing same no of *Pippalīs* on subsequent days for 10 days and then tapering dose by same no. of *Pippalīs* on following days till starting dose is achieved[4]. It has been advocated to be used in treatment of *Rājykṣma* by *Ācārya Suśruta*[5] and *Ācārya Kāśyapa*[6].

Material & Methods

Study Settings

The study was conducted in OPD/IPD of National Institute of Ayurveda, Jaipur & Ch. BrahmPrakash Ayurveda CharakSansthan, New Delhi. The patients receiving treatment from various DOTs centers were approached on person to person basis and those who voluntarily agreed to be part of study were included in study.

Aims & objectives:

To establish the efficacy of the *'VardhamānaPippalīRasāyana'* as an adjuvant therapyin the management of newly diagnosed cases of the Pulmonary Tuberculosis.

Inclusion criteria:

1. Age: 18 years to 7o years.
2. Sex: Both sexes.
3. Weight: >40Kg and <70 Kg.
4. Patients with newly diagnosed Pulmonary TB.
5. Patients able to produce sputum for bacterial culture and AFB (Acid Fast Bacillus) test.
6. At least two sputum specimens positive for acid fast bacilli (AFB) on direct smear microscopy.
7. Radiographic evidence suggestive of Pulmonary TB.
8. No prior history of TB or treatment with Anti- tubercular treatment (ATT).
9. HIV (Human Immunodeficiency Virus) negative.
10. Laboratory parameters done at or before the 14 days prior to screening (with results available to investigators for review) should fulfill the following conditions:
    a. ALT (Alanine aminotransferase) activity less than or equal to 2 times the upper normal limit**.**
    b. Total bilirubin less than or equal to 2 times upper limit of the normal.
    c. S. creatinine less than upper limit of the normal.
    d. Platelet count greater than 100,000/mm^3
11. Pregnancy test – Negative in case of female subjects.
12. Women with child bearing potential must agree to practice barrier method of the birth control or to abstain from heterosexual intercourse during the whole course of therapy.
13. Signed informed consent form to participate in study.
14. Ability to adhere to study and follow ups.
15. Firm home address & contact no. which is readily accessible during whole course of trial.

Exclusion criteria

1. Seriously ill and moribund patients.
2. The patients unlikely to survive for more than 6 months.
3. Patients diagnosed with or suspected of suffering from extra pulmonary TB.
4. Known history of any type of drug resistance TB.

5. Low lung reserve, marked tachypnoea, chronic corpulmonale, congestive cardiac failure.
6. BMI (Body Mass Index) less than 15.
7. Hypersensitivity to any of the drugs to be used in study.
8. Concomitantly taking any other *Āyurvedic* treatment for TB or any other disease.
9. Evidence of clinically significant metabolic, gastrointestinal, neurological or endocrinal diseases.
10. Abnormal renal functions.
11. Abnormal hepatic functions.
12. Malignancy.
13. Patients requiring surgical intervention in near future.
14. Known or suspected alcohol abuse that is sufficient to compromising safety or the cooperation of the patient.
15. Females who are pregnant, breast feeding or planning to conceive within the time frame described in the informed consent form.
16. Any major psychiatric illness.
17. Any pre-existing disease needing special interventions during the course of study.
18. Any pre- existing illness treatment of which has interactions with drugs employed in Anti-tubercular treatment**.**

Sampling Method:

Individuals presenting with the either signs & symptoms of Pulmonary TB described in modern medical literature or the signs & symptoms of the *Rājyakṣmā* described in any of the Āyurvedic classical literature will undergo following tests and procedures:

a) Complete medical history including Bio data of the patients.
b) Chief complaints.
c) History of present illness with origin duration and progress of each symptom.
d) History of past illness with treatments.
e) Personal history.
f) Family history.
g) Menstrual and obstetric history.
h) History of drugs and allergies.
i) Prior surgical history.
j) Interview about home, work and dietary habits.

i. Sputum collection to test for smear microscopy and culture.
ii. Montoux test.
iii. Chest X- Ray Posterio-anterior view.
iv. Blood draws for – CBC (Complete Blood Count), complete hematoogram, HIV testing, LFT (Liver Function test), KFT (Kidney function test).
v. Urine analysis – Routine

Sampling

The individuals who were registered at various DOTS centers were approached by investigator at personal level on the days of their visit to DOTS centre and those who voluntarily agreed to be part of study were interviewed extensively for their demographic profile, detailed history etc. Adult subjects fulfilling the inclusion criteria and devoid of any of the exclusion criteria were recruited for the study. The patients who were found suitable for the study after baseline investigations were randomized to receive one of the treatments specified in one of the research arms.

Total 516 patients were screened (interviewed) for registration in clinical trial. Out of 516 patients 213 patients were cases of extra pulmonary tuberculosis (ETB), patients were found to be relapse cases and 48 patients were found to failures of previous anti-tubercular treatment. So out of 516 cases screened 284 patients were out

rightly unsuitable to be enrolled for present clinical study.

Remaining 232 patients were newly diagnosed patients of pulmonary tuberculosis (PTB) but 89 patients turned out to be smear negative while remaining 143 patients were smear positive cases of pulmonary tuberculosis (PTB). Only these cases were primarily suitable for present clinical trial.

143 patients who were found suitable for present clinical trial were further evaluated for suitability of enrollment in present clinical study on basis of exclusion & inclusion criteria. Out of these 143 patients 79 patients could not be enrolled for various reasons.

So out of 516 patients screened only **64 patients** could be finally enrolled for study.

Randomization: 30 patients were recruited and randomly assigned to each treatment group for each group by simple randomization without any stratification.

Replacement: Four patients in each group left treatment in mid-way and did not co-operated in subsequent follow ups so they were replaced by four other patients in each group.

Sample size- 30 patients for each group

Study design:

The present study is

a. Single centre.
b. Open label.
c. Randomized.
d. Interventional type.
e. Efficacy & safety study.
f. With one group of active control.
g. Without any cross over.

The drugs, doses and schedule in each group of study was as follows

Group	Designated group	Assigned interventions
1	Active control group	Intensive phase of standard DOTS regimen for 8 weeks.
2	Experimental group	Intensive phase of standard DOTS regimen for 8 weeks *plus* *"VardhamānaPippalīRasāyana"*as per doses and schedule described in *Āyurvedic* classics.

Doses & administration of Treatment

Group1: DOTS regimen: As recommended in RNTCP program (2 HREZ+4 HR) in supervision of DOTS worker on alternate days of week).

Group 2: DOTS regimen As recommended in RNTCP program (2 HREZ/4 HR) in supervision of DOTS worker on alternate days of week. +***'VardhamānaPippalīRasāyana'***

Laghu Pippalīs of approximately uniform size were used in the treatment regimen.

The half of the total dose was administered in morning and other half in evening.

Pippalīs were taken as paste mixed with honey followed by milk.

The patients were advised to take full meal only after the drug was digested and they felt hungry.

They were also advised to abstain from heavy and spicy food.

Duration of treatment

19 days -for patients of initial body weight >60 kg

25 days for patients of initial body weight of 50-60 kg

36 days for patients of initial body weight of 40-50 kg

Follow up and assessment

Follow up of the patient to assess clinical improvement, drug compliance any adverse event was done weekly for two months i.e on days 7,14,21,28, 35, 42, 49 days. However, for statistical evaluation 28th day was chosen as cut off in all cases. This was done to avoid any ambiguity in results and any inconvenience in final analysis.

Lab monitoring for safety studies was planned to be done only in the cases where there would be necessarily required. However , as no serious adverse effect was observed in any of the patients no lab investigations were done in this regard.

Data Collection & Analysis

For valuation of efficacy:

1. **Conversion to sputum culture to negative states in each treatment group**.

   Proportion of the patients who turned AFB negative on smear microscopy on 28th day was statistically analyzed by using chi- square test.

2. **Reversal of the abnormalities of the hematogram in each treatment group.**

   Changes in Hemolobin (Hb gm%), Erythrocyte Sedimentation Rate (ESR) was analyzed by using t-test.

3. **Weight gain after the treatment**

   Change in the body weight was analyzed using t- test

Observations & Results

Total 516 patients were screened (interviewed) for registration in clinical trial. Out of 516 patients 213 patients (41%) were cases of extra pulmonary tuberculosis (ETB), 23(5%) patients were found to be relapse cases and 48 (9%) patients were found to failures of previous anti-tubercular treatment. So out of 516 cases screened 284 (55%) patients were out rightly unsuitable to be enrolled for present clinical study.

Remaining 232 patients (45%) were newly diagnosed patients of pulmonary tuberculosis (PTB) but 89 patients (17%) turned out to be smear negative while remaining 143(28%) patients were smear positive cases of pulmonary tuberculosis (PTB). (See Table 1)

Demographic profile of the patients

Out of 64 patients enrolled for study in present clinical trial 28 (48.75%) belonged to age group of 16-25 years, 13(20.31%) to age group 26-35. Together they formed about 70% of the patients enrolled for present study. Out of 64 patient who participated in present clinical trial, 36(56.25%) were males and 28 (43.75%) were females. Out of 64 patients who participated in clinical trial most of the patients (approx 97%) were educated up to or above senior secondary level. Only 3.12% patients were illiterate. 36 (56.3%) belong to lower middle income group followed by 23(35.9%) belonged to lower income group. 38 (59.4%) have permanent residence while 26 (40.6%) patients did not have their permanent residence were living in rented accommodations and were at place of study for their jobs. 33(51.6%) were non smokers. 9(14.6% o) took 6 to 10 sticks per day. 08(12.6%) took 11 to 15 sticks per day. 36 (56.3%) had no known history of TB in any family member or close associate whereas 28 (43.7%) of the patients had known history of TB in family member or close associate. 37 (57.8%) had no previous history of recurrent upper respiratory tract infections whereas 27 (42.2 %) patients gave positive history. (See Table 2)

Pattern of consumption of *pippalīs*

As shown in figure 1for a person of body weight of 40-50 kg, 36 days were required to complete therapy. 1026 *pippalīs*were consumed during this period. Maximum dose was achieved on day 18 after starting

therapy. 54 *pippalīs*weighing 13.5 gm (approx) were taken on this day. Daily dose was divided in 2 or 3 equal parts to be taken two times or three times a day, as per convenience of patient. once the dose > 6 mg/day was achieved. 256 g (approx) *pippalīs*were consumed during course of therapy.

For a person of body weight of 50-60 kg, 25 days were required to complete therapy. 1014 *pippalīs* were consumed during this period. Maximum dose was achieved on day 13 after starting therapy. 78 *pippalīs*weighing 19.5 gm (approx) were taken on this day. Daily dose was divided in 2 or 3 equal parts to be taken two times or three times a day, as per convenience of patient, once the dose > 6 mg/day was achieved. 253 g (approx) *pippalīs*were consumed during course of therapy.

For a person of body weight of >60 kg, 19 days were required to complete therapy. 1000 *pippalīs* were consumed during this period. Maximum dose was achieved on day 18 after starting therapy. 100 *pippalīs*weighing 25 gm (approx) were taken on this day. Daily dose was divided in 2 or 3 equal parts to be taken two times or three times a day, as per convenience of patient, once the dose > 6 mg/day was achieved. 250 g (approx) *pippalīs*were consumed during course of therapy.

Effect of Therapy on AFB Positivity

Before treatment, in group 1, 10(33.3%) patients had AFB positivity of grade 3, 13(43.3%) patients had AFB positivityof grade 2, 7(23.3%) patients had AFB positivityof grade 1 and 0(0%) had AFB positivityof grade 0; whereas, in group2, 10(33.3%) patient had AFB positivityof grade 3, 12(40%) patients had AFB positivityof grade 2, 10(33.3%) patients had AFB positivityof grade 1 and 0 (0%) had AFB positivityof grade 0.

Intergroup comparison before treatment, revealed Pearson Chi square value to be .107 and significance level of .948 ($p>0.05$) which means there was no statistically significant difference between group 1 & group 2, before treatment.

After treatment data shows; in group 1,0(0%) patients had AFB positivityof grade 3, 6 (20%) patients had AFB positivityof grade 2, 12(40%) patients had AFB positivityof grade 1 and 12(40%) had AFB positivityof grade 0; whereas, in group2, none (0%) had AFB positivityof grade 3, 5 (16.7%) had AFB positivityof grade 2, 3(10%) had AFB positivityof grade 1and 22(73.3 %) had AFB positivityof grade 0.

Intergroup comparison after treatment, revealed Pearson Chi square value to be 8.432 and significance level of .015 ($p<0.05$) which means there was statistically significant difference between group 1 & group 2 after treatment.

However, as in group 2, as there were 22(73.3%) patients who had AFB positivityof grade 0, 3(10%) in grade 1 and 5(16.7%) in grade 2and none (0%) in grade 3 in comparison to 12(40%), 12(40%), 6 (30%) and 0(0%) of group 2 respectively; treatment 2 was found to be more effective than treatment 1.(see table 3)

Effect of therapy on Hemoglobin (Hbgm%)

As table 4 shows that mean hemoglobin before treatment (Hb_BT) was 10.5 gm% (SE of = 0.26) in group 1 and 9.7 gm% (SE = 0.20) in group 2. An independent t- test revealed that t value was 2.306. 2- tailed significance of this t- value at 58 df is 0.02 ($p<0.05$) which means there is significant difference in hemoglobins of the patients of group1 and group2.

It also shows that mean hemoglobin after treatment (Hb_AT) was 11.5 gm% (SE= 0.21) in group 1 and 11.7 (SE=0.18) in group 2. An independent t- test revealed t value was 0.697. 2 tailed significance of this t- value at 58 df is 0.48 ($p>0.05$) which means there is no significant difference in

hemoglobin levels of both groups after treatment.

Mean of difference of Hb gm%, before & after treatment was also calculated which was found to be 0.9 (SE=0.9) in group 1 and 1.9 (SE=0.09) in group 2. Calculated t-value was 7.971. 2- tailed significance of this value at 58 df is 0.001 ($p<0.01$) which means there is highly significant difference between both groups.

It can be inferred from above findings that treatment given to group 2 patients has more effect in improving Hb gm% levels.

Effect of therapy on estimated sedimentation rate (ESR) in first hour

Mean ESR before treatment (ESR_BT) was 34.8 (SE of =1.47) in group 1 and 38.6 (SE = 1.52) in group 2. An independent t- test revealed that t value was 1.80. 2- tailed significance of this t- value at 58 df is 0.07 ($p>0.05$) which means there is no significant difference in ESR of the patients of group1 and group2 before treatment.

Mean ESR after treatment (ESR_AT) was 21.8 (SE= 0.939) in group 1 and 19.0 (SE= 1.02) in group 2. An independent t- test revealed t value was 2.06. 2- tailed significance of this t- value at 58 df is .04 ($p<0.05$) which means there is significant difference in hemoglobin levels of both groups after treatment.

Mean of difference of ESR before & after treatment (ESR BT_AT) was also calculated which was found to be 13.6 (SE=.95) in group 1 and 18.6 (SE=1.13) in group 2. Calculated t-value was 3.40. 2-tailed significance of this value at 58 df is 0.001 ($p<0.01$) which means there is highly significant difference between both groups.

It can be inferred from above findings that treatment given to group 2 patients has more effect in improving ESR levels. (see table 5)

Effects of Treatment on Body weight

Mean body weight before treatment (Bwt_BT) was 45.93 (SE of =1.30) in group 1 and 47.20 (SE = 1.33) in group 2. An independent t- test revealed that t value was .677. 2- tailed significance of this t- value at 58 df is 0.501 ($p>0.05$) which means there is no significant difference in ESR of the patients of group1 and group2 before treatment.

Mean body weight after treatment (Bwt_AT) was 47.30 (SE= 1.33) in group 1 and 49.83 (SE= 1.31) in group 2. An independent t- test revealed t value was 1.352. 2- tailed significance of this t- value at 58 df is .182 ($p>0.05$) which means there is no significant difference in hemoglobin levels of both groups after treatment.

Mean of difference of body weight before & after treatment (Bwt BT_AT) was also calculated which was found to be 1.37 (SE=.18) in group 1 and 2.83 (SE=1.17) in group 2. Calculated t-value was .5.723. 2-tailed significance of this value at 58 df is 0.001 ($p<0.01$) which means there is highly significant difference between both groups.

It can be inferred from above findings that treatment given to group 2 patients has more effect in improving body weight.

Discussion

*Pippali*is a specially recommended *rasāyana* for respiratory system (*Prāṇavahasrotasa*) and for *Kaphadoṣa*.It promotes expectoration and thus used for coughs, colds, bronchitis, asthma, wet and 'mucousy' conditions of the lungs. It is a known rejuvenative for the lungs. It encourages vasodilatation and therefore increases circulation, specifically to the lungs .It is used with honey in asthma, bronchitis, laryngitis, pneumonia and compromised immunity in the respiratory system to reduce *kapha*. It is also used to treat mild fever by removing the *ama*from *rasa dhātu*and alleviating the concurrent

aches in the muscles and joints (Brawley& Lad 1994). The herb is known to stimulate *agni*and strengthens weak digestion.

Kurup et al (1979) reported that some of the compounds isolated from *Pippalī* to possess anti-tubercular activity.

In an experiment it was concluded that *Mycobacterium smegmatis*(non-tuberculous bacteria) was found to be sensitive against chloroform (PC), ethanol (PE), ethyl-acetate (PEA) and hexane (PH) extracts of fruits of *Piper longum*. The mean minimum inhibitory concentration (MIC) of different extracts were in the increasing order of PC>PE=PH>PEA. MIC of PC, PH, PE, PEA was found to be 8, 16, 16 and 32 mg/mL, respectively and minimum bactericidal concentration (MBC) was calculated as 20.23, 33.43, 36.23 and 64.09 mg/mL, respectively. Chloroform extract of *Piper longum*(PC) showed the highest *in vitro* antioxidant activity aswell as antimycobacterial activity. So the anti-microbial activity of *pippalī* must be responsible for faster and better reversibility of AFB positivity in patients of pulmonary tuberculosis[1]. Reduced bacterial load may also be responsible for significant reduction in ESR.

A number of in-vitro studies have proved that *pippali*is an effective hepato-protective activity as it increases reduced glutathione level and decreases lipid per oxidation level[2]. The hepatoprotective effect of *Piper longum*is comparable to the standard drug silymarin (25 mg/kg/day p.o. for 21 days)[3]. The hepatoprotective and stimulant actions must be responsible for significant improvement in Hemoglobin and weight of the tubercular persons.

Strength of study

64(12.4%) patients were recruited after screening of 516 patients. So the sample has fair chance of being true representative of actual scenario.

It is established by this study that *'PippaliVardhmānaRāsayana'* is effective adjuvant to DOTs therapy as faster cure of symptoms, faster achieving of AFB negativity, better improvement in body weight, Hemoglobin level, TLC and *ojus* score is achieved.

The treatment is of short duration so there are fewer chances of dropouts.

The drug is harmless, can be self-administered and does not need any specific monitoring or supervision. The drug is available at every nook and corner of India and whole treatment cost is <1000 INR.

The study focuses on analysis of pathogen but host factors also so it provides better understanding of control of disease and efficacy of drugs.

Limitations of study and further suggestions

It was open single centered study on sample size of 30 patients in each group. To generate higher quality of evidence a double blind multi-centered study should be planned.

Out of 64 patients enrolled in present clinical trial, 70% patients were below age of 35 years while 30% patients were above age of 35years.So the results may be best applicable for this population group only. Further trials may be planned in such a manner that there could be uniform

representation of different population groups.

Present clinical study was planned to evaluate efficacy & safety of *'PippalīVardhmānaRasāyana*' on newly diagnosed smear positive patients of pulmonary tuberculosis (PTB). During trial it was observed that a large section of patients suffers from extra pulmonary tuberculosis (ETB) also. So a separate study may be planned to evaluate efficacy & safety of *PippalīVardhmānaRasāyana*' for patients of extrapulmonary tuberculosis.

HIV and diabetes are two most common diseases which are associated with the suppression of cell mediated immunity and are known to increase risk of developing TB. It is estimated that by 2030, 42% of smear positive cases in India will be attributable to diabetes. Patients of smear positive TB with diabetes & HIV infection were excluded from this study. Separate studies are needed to evaluate efficacy and safety of *ayurvedic*drugs in these patients.

MDR, XDR & XXDR cases are increasing day by day and are matter of worry for future TB strategies. Studies must be planned to identify effective drugs for prevention and treatment of such cases. *'PippalīvardhmānaRasāyana'* may emerge as good choice.

Conclusion

'Pippalī Varhmāna Rasāyana' along with DOTS is more effective for conversion of AFB smears to negative states, improvement in Hb gm%, improvement of body weight and normalization of ESR which corresponds with improvement of subjective feeling of well being. So, it is a promising drug for management of Pulmonary Tuberculosis.

Table 1 Description of 516 Patients Screened For Clinical Trial

S.No.	Category	Number	Percentage (%)
1.	Smear positive pulmonary tuberculosis (PTB)	143	28
2.	Smear negative pulmonary tuberculosis (PTB)	89	17
3.	Extra-pulmonary tuberculosis (ETB)	213	41
4.	Relapse Cases	23	5
5.	Others (failures etc.)	48	9
	Total	516	100

Table 2 Demographic Characteristics of the patients enrolled for study

Profile	Particulars	Numbers	Percentage (%)
Age Group	16- 25 Years	28	43.75
	26-35 Years	13	20.31
	36-45 Years	5	7.81
	46-55 Years	6	9.37
	56-65 Years	8	12.50
	66-75 Years	4	6.25
Gender	Male	36	56.25
	Female	28	43.75

Educational Status	Illiterate	02	3.12
	Primary Education	00	00
	Senior Secondary	12	18.75
	Matriculation	28	43.75
	Graduation	17	26.56
	Post Graduation	05	7.81
Socioeconomic Status	Lower	23	35.9
	Lower Middle	36	56.3
	Upper Middle	05	7.8
	Higher	00	00
Residential Status	Migratory	26	40.6
	Permanent Residents	38	59.4
Smoking	None	33	51.6
	0 to 5 Sticks	02	3.1
	6 to 10 Sticks	09	14.0
	11 to 15 Sticks	08	12.6
	16 to 20 Sticks	10	15.6
	>20 Sticks	02	3.1
Proximity to TB Patient	Present	28	43.7
	Absent	36	56.3
H/O URTI	Present	27	42.2
	Absent	37	57.8

Table 3 Effect of Treatments on AFB positivity

Grade	Before Treatment (BT)		After Treatment (AT)	
	Group 1(n=30)	Group 2 (n=30)	Group1(n=30)	Group2(n=30)
0 (Negative)	00	00	12	22
1(+1 positive)	07	08	12	03
2 (+2 positive)	13	12	06	05
3 (+3 positive)	10	10	00	00
P.Chi Square Value	.107		8.432	
df	2		2	
p-value	.948		.015	
Significance	Not significant		Significant	

Table 4 Effects of Treatment on Hb gm %

Groups		Mean gm%	SE	Independent sample t-test (assuming equal variances)					
				df	t-value	Sig. (2-tailed)	Mean dif	95%CI	
								Lower	Upper
BT	Group1(n=30)	10.5	0.26	58	2.306	0.02 ($p<0.05$) (S)	.77	.10	1.4
	Group2(n=30)	09.7	0.20						

AT	Group1(n=30)	11.5	0.21	58	.697	0.48 (p>0.05) (NS)	.28	.77	.37
	Group2(n=30)	11.7	0.18						
Diff.	Group1(n=30)	0.9	0.07	58	7.971	0.001 (p<.01) (HS)	.97	1.2	.72
	Group2(n=30)	1.9	0.09						

Table 5 Effects of Treatment on Erythrocyte Sedimentation rate in 1st hour (ESR)

Groups		Mean (mm/1h)	SE	Independent sample t-test (assuming equal variances)					
				df	t-value	Sig. (2-tailed)	Mean dif	95%CI	
								Lower	Upper
BT	Group1(n=30)	34.8	1.47	58	1.80	.07 (p>0.05) NS	3.83	8.90	.42
	Group2(n=30)	38.6	1.52						
AT	Group1(n=30)	21.8	.939	58	2.06	.04 (p<0.05) S	2.86	.08	5.65
	Group2(n=30)	19.0	1.02						
Diff.	Group1(n=30)	13.6	.95	58	3.40	.001 (p<0.01) HS	5.03	7.99	2.07

Table 6 Effects of Treatment on Body weight

Groups		Mean (kg)	SE	Independent sample t-test (assuming equal variances)					
				df	t-value	Sig. (2-tailed)	Mean dif	95%CI	
								Lower	Upper
BT	Group1(n=30)	45.93	1.30	58	.677	.501 (p>0.05) NS	1.267	5.01	2.47
	Group2(n=30)	47.20	1.33						
AT	Group1(n=30)	47.30	1.33	58	1.35	.182 (p>0.05) NS	1.87	6.82	1.21
	Group2(n=30)	49.83	1.31						
Diff.	Group1(n=30)	1.37	.18	58	5.72	.001 (p<0.01) HS	1.46	1.98	.95

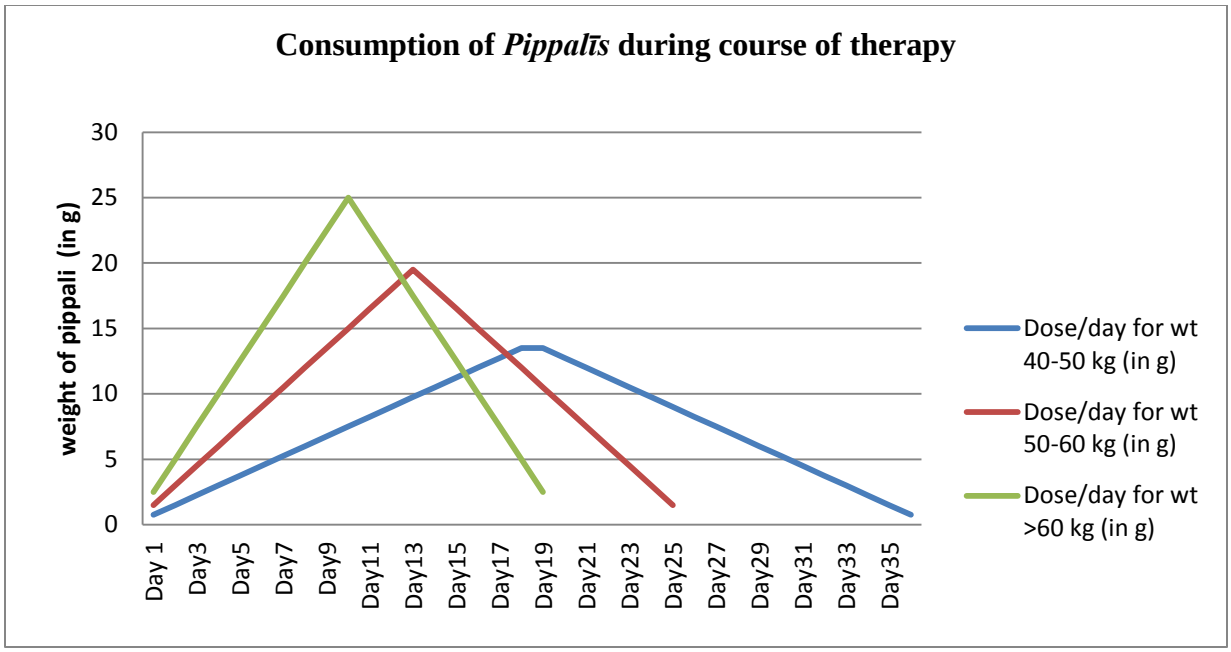

Figure 1:Consumption of *Pippalīs* during course of therapy

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