Project Report

“Evaluation of Nootrophic (Cognition Enhancing) Effect Of Shankhapushpi (Convolvulus Prostatus forssk\Syn: Convolvulus Pluricalaulis Choisey) In Slow Learners”

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Supported by

Ministry of AYUSH, AYUSH Bhawan, B-Block, GPO Complex, INA, New Delhi-110023
PROGRESS REPORT

Project Sanctioned By
Central Council for Research In Ayurveda & Siddha,
Dept. of AYUSH,

PROJECT TITLE
EVALUATION OF NOOTROPHIC (COGNITION ENHANCING) EFFECT
OF SHANKHAPUSHPI (Convolvulus Prostata forssk\SYN. Convolvolus Pluricalaulis Choisy) IN SLOW LEARNERS.

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SUBMITTED BY
Centre for Post Graduate Studies & Research in Ayurveda,
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Pune- 411011.
2009-2011
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Evaluation of Nootrophic (Cognition Enhancing) Effect Of Shankhapushpi (*Convolvulus Prostatus forssk\Syn: Convolvulus Pluricalaulis Choisey*) In Slow Learners

### 1. Title of the Project

### 2. Principal Investigator:

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5. Other Non-Scientific Staff Engaged in the Study:

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   Mr. Ganesh Herekar

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Supervisor & School Committee Member, Boy’s High school

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Assistant Teacher, Boy’s High school

Mrs. Shobha Nikam
Head Mistress, Girl’s High school

Mrs. Asha Sonavane
Head Mistress, Primary school

Mrs. Vaishali Patil
Assistant Teacher, Primary School

6. Implementing Institution:

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583/2, Rasta Peth,
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7. Other collaborating Institutions:

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   Modern Girl’s High School
   Modern Primary School

2. Seth Tarachand Ramnath Ch. Hospital,
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2. Nisarga Biotech, Chandanagar, M. I. D. C. Area, Satara
8. Date of commencement:

1st June 2009

9. Duration of Project:

2 Years

10. Date of completion:

31st May 2011

11. Introduction:

Ayurveda is the oldest system of Medicine in the world, its antiquity going back to the Vedas. It adapts a unique holistic approach to the entire science of life, health and cure. The areas of special consideration in Ayurveda are geriatrics, rejuvenation, nutrition, immunology, genetics and higher consciousness.

In the competitive era of modern civilization intellect is the navigator of futuristic carrier in school going children. This is directly reflected in the form of learning skills, however astonishingly according to the epidemiological survey the substandard levels of learning skills (slow learning) i.e. relatively hampered reading, writing & mathematical are present in 8% of school going children.(ref) When children live in impoverished or neglectful home environments, enriching preschool programs and other forms of early intervention can make an appreciable difference. For instance, high-quality child care and preschool programs (e.g., Head Start) frequently lead to short-term IQ gains and other cognitive and academic benefits. Early intervention is most effective in fostering intellectual development when it is tailored to children’s existing abilities and interests.
The very act of attending school leads to small increases in IQ. In Western societies, children who begin their educational careers early and attend school regularly have higher IQ scores than children who do not.

Obdiviously, this problem is seen to be the major obstacle in the carrier of the above-mentioned population in India. On the other hand where management of such prevalent psychological problem, which has wide impact of social imbalance, is concerned, even the modern psychiatry depends upon the educational intervention compensation, strategies and motivational support. (Ref)

The medication therapy is yet to be established with concert base and that is why Rasayan chikitsa now becomes more important as far as medical intervention in management of above-mentioned psychological problem is concerned.

The Ayurvedic texts describe a set of rejuvenative measures to impart biological sustenance to the bodily tissues. These remedies are called Rasayana which are claimed to act as micronutrients. Some of these Rasayanas are organ and tissue specific. Those specific to brain tissue are called Medhya Rasayana. Such Rasayanas retard brain aging and help in regeneration of neural tissues besides producing antistress, adaptogenic and memory enhancing effect. In addition to the long tradition of textual and experience-based evidence for their efficacy, certain recent studies conducted on these traditional remedies on scientific parameters have shown promising results which have been reviewed to provide a lead for further studies.

Madhya rasayanas is a group of rasayan drugs mentioned in Ayurveda, which improve function of faculties of intellect as well as mind. Since ages these drugs are used in management of psychiatric and psychosomatic disorders however the scientific clinical trials are necessary to reestablish their specific Nootropic effect. (Singh, R.H) ¹

Among the various Medhya rasayan drugs, Shankhapushpi is the most important due to its broad spectrum effect. Shankhapushpi or Convolvulus Pluricaulis is an indigenous plant which is mainly advocated for use in mental stimulation and rejuvenation therapy. The popular Medhya Rasayanas are Ashwagandha (Withania somnifera Dunal), Brahmi (Bacopa monnieri Linn), Mandukaparni (Centella asiatica Linn) and Sankhapuspi (Convolvulus pluricaulis Chois). (Kumar V. et al)²
The plant was considered as one of the best of mental rejuvenators by Caraka. This plant has action on CNS and is well established Nootropic drug and several publications have been appeared in last two decades validating its Nootropic effect and shows neuronutrient impact in brain ageing (Singh Ram Harsh et al)³

Shankhapushpi is quoted in charka to be the single greatest herb for enhancing all three aspects of mind power learning (Dhi), Memory (Dhriti), and recall (smriti). Thus it is called the greatest Medhy Rasayan (that which enhances the mind power) It helps the quality of sleep by improving mind body coordination. It is proved that Convolvulus Pluricaulis shows enhancement of memory (Dhriti) and significantly higher percent retentions (smriti). (Sharma et al)⁴ Convolvulus pluricaulis possesses neuroprotective potential (Bihaqi SW)⁵ Convolvulus pluricaulis elicited a significant antidepressant-like effect in mice by interaction with the adrenergic, dopaminergic, and serotonergic systems (Dhingra D)⁶ Convolvulus pluricaulis shows the acetylcholinesterase inhibitory activity (Vinutha, B. et al)⁷

Shankhapushpi can be used to produce alterations in the general behaviour pattern, reduction in spontaneous motor activity, hypothermia, potentiation of pentobarbitone-sleeping time, reduction in exploratory behavioral pattern, and suppression of aggressive behaviour. (Subhangi A. Pawar et al)⁸ Shankhapushpi is very beneficial for nervous system enhancing the quality of Bone marrow & nerve tissue (Majja dhatu). (Ref). The petal extract of Shankhapushpi exerted antianxiety effect in mice on elevated plus maze. (K. Sharma et al)⁹ Convolvulus pluricaulis significantly improved learning and memory, reversed the amnesia and shows the Nootropic activity. (Nahata, Alok; et al)¹⁰ Shankhpushpi is a prominent memory improving drug, a psychostimulant and tranquilizer in traditional Indian medicine. The plant contains alkaloids convolvine, convolamine, phyllabine, convolidine, confoline, convoline, subhirsine, convosine, and convolvidine along with scopoline and β-sitosterol. It is one of the four drugs (Convolvulus pluricaulis, Evolvulus alsinoides, Clitoria ternatea, and Canscora decussata) described in Ayurveda as Shankhpushpi. C pluricaulis is described and used as Shankhpushpi by most practitioners (Kapadia NS et al)¹¹
Apart from acting as Medhya (brain tonic), Shankhpushpi is indicated as digestive, appetite stimulant, carminative for digestive system and also a deworming agent. (4 & ayu literature) It has cardio-protective, heart strengthener and controls hypertension. It is used in Ayurvedic formulations for chronic cough as it has mucolytic properties thus helps in chest congestion. It is a proved spermetogenic and strengthens urogenital system. It is a common ingredient of Ayurveda based herbal hair oils as it helps to stimulate hair growth. It is used in Ayurvedic formulations meant for sleeplessness, epilepsy, hallucinations and anxiety. In Ayurveda it is indicated for general debility and is a known Rasayana herb. (Ch.Ch.Adyaya 1).

Administration of Convolvulus pluricaulis decreases serum T3 concn. and the activity of hepatic 5'-DI and G-6-phase, without marked alteration in hepatic lipid peroxidn., indicating the possible regulation of hyperthyroidism. Inhibition of T3 production in levothyroxine-treated female mice by the root extract of Convolvulus pluricaulis, Panda, S.; Kar, A., Hormone and Metabolic Research 33(1), 16-18, 2001.

Shankhpushpi is used in many formulations in Ayurveda. Main formulations containing Shankhpushpi are: Shankhpushpi panaka, Medhya kashay. (Ref) Different institutions & industries have conducted clinical trials to asses its Medhya effect in various conditions. However, its efficacy in slow learning children was not been proved yet.

These problems in children affect entire carrier & productivity in younger generation; hence it is necessary to concentrate on positive mental health in this group, as per Hindu mythology ritual of ‘vratabandhan’ (thread ceremony) is performed at the age of 8 as it is believed that at the age of 8 child is enough matured to enter in his scholastic carrier.

It was there-for considered appropriate to undertake clinical evaluation of Nootropic effect of Shankhapushpi based product in slow learner amongst the children of age group of 6 to 13. Also, as per the findings from the previous study on Shankhapushpi, one open label pilot study was carried out as the appendix of this study. The main aim was to observe the effect of Shankhapushpi on neurotransmitters. The results obtained from the study are attached with this report. (Appendix A):

2. Ethics:
2.1 Institutional Ethics Committee:
All the study documents were submitted to Institutional Ethics Committee. Ethics committee nominee had reviewed all documents. After due scrutiny of the project, the committee has found that the protocol has been prepared according to the ethical principles of the Declaration of Helsinki, ICH-GCP. The committee granted permission to conduct the said project. The letter of Ethics Committee approval is given in *Annexure I*.....

2.2 Ethical Conduct of the Study:
The study was conducted as per ethical principles of the Declaration of Helsinki, ICH GCP guidelines and Indian regulatory and ethical guidelines (‘Guidelines for Clinical Trials on Pharmaceutical Products in India– GCP Guidelines’ issued by Central Drugs Standard Control Organization (CDSCO), Ministry of Health, Government of India in 2005; ‘Requirements and guidelines for permission to import and / or manufacture of new drugs for sale or to undertake clinical trials’ (Schedule Y, 2005); and ‘Ethical Guidelines for Biomedical Research on Human Subjects’ issued by Indian Council of Medical Research in 2000).

2.3 Blinding:
The subjects were enrolled in a double blind, randomized fashion. At the initiation of a study, the site was instructed on method of blind breaking. It was also explained to open the blinding codes in emergency situation for reason of subject safety. The investigator was encouraged to contact Nisarga Biotech Pvt. Ltd. before breaking the blind. **However, no blind breaking was required throughout the trial.**

3. **Experimental work:**

3. I **Experimental set up:**

3. I.1. Site & sample preparation
• Project was started after appointment of qualified staff through interview which was held on 8th May.

• Exclusive set up with separate cabin having Advanced Computer System, necessary Furniture including storage facility required for Shankhapushpi Research Project was arranged by CPGS & RA.

• Staff is appointed from 1st June.

• **Staff GCP training** – This study includes drug trial on the Human Participants. Ethical issues are important in human trial. Hence before starting the actual work of the project, GCP (Good Clinical Practice) training was given to the scientific staff with the help of experts. **GCP trained staff is the big asset for the project.**

• Progressive Education Society’s Modern Boys High school, Modern Girls High school & Modern primary school were selected for clinical trial & NOC was obtained from school Principals.

• Three meetings of teachers were held for explaining T.Q. & 400 students were recruited on the basis of procured T.Q from teachers.

• Parents Meeting of 400 students, recruited was organized.

• Informed Consents from 230 parents were obtained in this meeting.

3. I. 2. **Preparation of drug was done**

• Various samples were collected for the authentic sample of Shankhapushpi (Convolvulus Pluricalaulis Choisey) from different geographical locations & sources.

• All samples were identified & authenticated with the help of taxonomist & Dept. of Botany of Agharkar Research Institute, Pune.

• Only two samples were authentified as Convolvulus pluricalaulis choisey within the standard limits of API

• The sample which was supplied by Nisarga Biotech, Satara was selected & ghana was prepared & was standardized (**Annex II**).

• Capsules filled with Shankhapushpi ghana (70 mg) were prepared as per GMP norms

• Bottles were filled & labeled as per Good Labeling Practices.

• Identical capsules & bottles of placebo were also prepared
3. I. 3. Preparation of trial related documents (From June 09 to Oct.09)

- Latest review & monograph of Shankhpushpi was prepared.
- As no standard version of suitable Questionnaire is available for identifying slow learners from class, a teachers Questionnaire is developed & standardized with the help of consultant psychologist which could give correct assessment in which each question had given rating 1, 2, 3 etc. (Annex. IV)
- For the feedback from parents, a Parent’s Questionnaire for slow learners was prepared with the help of consultant psychologist. (Annex. V)
- Parent’s Consent form in English as well as in Marathi was prepared. (Annex. VI)
- Project Information sheet in English as well as in Marathi was prepared. (Annex. VII)
- A Performa was prepared incorporating socio demographic background information for slow learners. (Annex. VIII)
- For determination of exclusion criteria, Proforma for psychiatric evaluation was developed with the help of consultant neuropsychiatrist.(Annex.IX)
- Case Record Form was prepared with the help of consultant Ayurved physician for the thorough assessment of students as per protocol. (Annex. X)
- ADR form was prepared (Annex. XI)
- Follow-up shits for monthly Follow-ups (Annex. XII)
- Drug dispensing logs & Drug accountability logs were prepared according to planned schedule of dispensing.

4. Objectives:

4. 1 Primary Objective

1. To assess the efficacy and safety of Shankhpushpi in slow learners of age group 6-13 years.
2. To evaluate Nootropic effect of Shankhpushpi Ghana as a Medhya Rasayana.

4. 2 Secondary objective

1. To assess clinical outcome and relationship between the clinical, biochemical and psychological end points of the study treatment.
2. To identify the correlates of outcome with the psychometric profile.
5. Methods Adopted:
(Annex. XIII)

5. I. Trial Design:
Methodology followed was as per protocol (Annex) which is as follows:
No modifications are made.
A description of the type /design of trial to be conducted (e.g. double blind, placebo controlled, parallel design) and a schematic diagram of trials design, procedures & stages.
- Prospective
- Double blind
- Placebo controlled
- Parallel design

End Points:

Primary End Point:
- Change the base line in scholastic performance
- Improvement in reading, writing & mathematical skill as shown linguistic, mathematical, motor, social and behavioral performance Etc.

Secondary end point:
- Change from baseline in IQ, verbal and performance scale.
- Change from baseline in child behavior profile
- Change from baseline in social adjustment
- Improvement in mental status of the patients as per Ayurvedic guidelines

Safety end point:
- Considerable change in baseline laboratory investigations

5. II. Criteria for Selection and withdrawal of subjects: (Annex. XIV)

171 Patients were recruited in the study.
Patients included in the study only after they met all the inclusion criteria and exhibited none of the exclusion criteria mentioned below.

5. II.1. Inclusion Criteria:

- Children admitted in the school of age group 6 to 13 years of either sex
- Children screened as slow learners as per clinical examination.
- Consistent academic underperformance – last 2 year or more years.
- Consenting parents

5. II.2. Exclusion criteria:

- Any past or present psychotic symptoms
- IQ below 70 (mentally retarded or subnormal children.
- Past head injury warranting hospitalization
- Any major medical illness
- Congenital anomalies like Down syndrome
- Uncorrectable sensory handicap
- Current antiepileptic medication
- The patients who have used any other investigation drug one month prior to start of study treatment.
- Use of any other immunomodulatory drug one month prior to start of study treatment.

5. II.3. Subject withdrawal criteria: -

- Patient wishes to discontinue the treatment during trial treatment.
- Patient is lost to follow up for 2 consecutive visits.
- Serious adverse reaction and stage 3 toxicity is developed.
- Patients who were withdrawn subjects were followed same as the treatment groups.

5. III. Criteria for Evaluation:

5. III.1. Efficacy Evaluation:

- Clinical examination
- IQ
- Child Behavior Checklist
Clinical Examination:
Clinical examination includes physical (Systemic examination- Skin, HE/ENT, Respiratory system, CVS, CNS & Abdominal) and vital examination (Pulse rate, Respiratory rate, Blood Pressure, Weight, Height & Abdominal girth) along with general examination by Ayurvedic methods. (Dashavidha & Ashtavidha Pariksha) to exclude the presence of any major systemic disease/disorder

Intelligent Quotient (I.Q) Testing (Wechsler’s Intelligence Scale for Children): (Annex XVI)
Although low IQ per se is not directly related to Slow Learners, if the child is considered as Slow Learner, It may show the some clues in IQ level. Information, general comprehension and many other abilities are checked in assessing an IQ. Inattentive and hyperactive child may be compromised in these areas and it will be reflected in the IQ scores. Having brought the attentiveness and having settled the hyperactive child may lead us to his/her ‘original’ IQ, which is higher than the previously hyperactive and inattentive child. Before initiation of the study the IQ assessment was done to exclude the retarded children.

Constructed after the general model of the popular American test of Dr. David Wechsler’s Intelligence Scale for Children, better known by the acronym WISC. The Indian scale by Dr. Arthur J. Malin of Nagpur embraces all the advantages of the Original along with what is hoped are several improvements.

Two main reasons for the preference for the WISC are the simplicity of its administration and its analytical breakdown into factorial functions for vocational and educational guidance.

The original WISC as well as its Indian adaptation works on the Point Scale and all items of a given type are grouped together and arranged in increasing order of difficulty.

Vocabulary tests in intelligence scales perform a dual role; one, as a test of ‘verbal
Comprehension” and another as a test of “verbal information”. From various data, it is clear that the verbal comprehension factor of the vocabulary test operates on the lower age levels and the verbal information factor on the upper age levels.

The headings under which the test is performed are:

1. Information test
2. General comprehension test
3. Arithmetic test
4. Analogies and Similarities
5. Vocabulary test
6. Digit span test
7. Picture completion
8. Block design
9. Object assembly
10. Coding and
11. Mazes


The child Behavior Checklist (CBCL) is a device by which parents or other individuals who know the child well rate a child’s problem behaviors and competencies. The child behavior checklist for ages 6 to 18. It consists of 113 items related to behavior problems which scored from 3 point scale ranging from not true to often true of the child. There are also 20 social items used to obtain parents report of the amount of quality of their child participation in sport, hobbies games activities organization, jobs and friends how well the child gets along with others & play & works by himself/herself & school functioning. This instrument can either be self-administered or administered through an interview. The CBCL can also be used to measure a child’s change behavior over time or following a treatment.

It can be scored in terms of two broad grouping of syndromes. One grouping is designated as ‘Internalizing’. This grouping is called ‘Internalizing’ because it comprises problems that are mainly within the self. The second grouping, designated as ‘Externalizing’ because
it comprises problems that are mainly involve conflicts with other people and with their expectations for the child. The internalizing is easily computed by summing the scores for the three internalizing syndromes and the Externalizing score is computed by summing the scores for the two Externalizing syndromes. Third one is Total Problem score is readily computed by summing the scores for Internalizing, Externalizing, the other three syndromes, and the other problem are not on any of the syndrome.

Competence score- mal adaptive behavior is indicated by low score on the competence scale & high score on the problem scale. The activities, social & school scales are summed to yield total competence score.

**Mini Mental Status Examination: (Annex. XVIII)**

The Mini Mental Status Examination (MMSE) is an appropriate tool to assess Medha (grasping, retention & recall). It involves assessment of following parameters:

  1) Orientation of time
  2) Orientation to place
  3) Immediate recall
  4) Attention
  5) Delayed verbal call
  6) Naming
  7) Repetation
  8) 3-stage command
  9) Writing
  x) Copying

**Adjustment Inventory for school going children (By Jnana Prabodhini’s Institute of Psychology, Pune): (Annex XIX)**

This test is based on Bell’s school Inventory, which indicates the level of adaptation with the school environment. It can be conveniently used for screening adolescent school students.

A high score on this test indicates a high level of adaptation with the school environment. Students with high scores like their teachers, enjoy school life, are happy with their
schoolmates & feel that the school is conducted systematically & fairly. The poorly adapted students with low scores dislike their teachers, have complaints about school life & schoolmates & feel that they get an unfair treatment in the school. They may express a desire to withdraw from school.

**Mental Examination by Ayurveda: (Annex XX)**

A detailed Proforma for mental status examination on Ayurvedic guidelines was prepared and used to assess the effect in mental faculties. The gradation was given as per guidelines given by Proforma for mental status examination on Ayurvedic guidelines by NIMHANS, Banglor. The improvement was assed as per improvement in gradations

Gradition- Pravara-3

Madhyam-2

Avar-1

The characters asssed are objects of mind i.e. Chintya (to be thought about), Vicharya (Questionable, to be discussed), Oohya (Speculation), Dhyeya (Objectives), Sankalp (to determine)

**5. III. 2. Safety Evaluation:**

- Clinical examination for adverse events
- Hematological Investigations include Complete Blood Count, Liver Function Tests, Renal Function Tests, Urine Examination.
- ECG

**Clinical Examination for adverse events: (Annex. XI)**

To assess the safety of the study drug, adverse events occurred during the subject participation were captured. Following definitions are used for adverse events.

**Adverse event:** Any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign, symptom, or disease (including an abnormal finding), temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal
(investigational) product. Subjects will be asked to notify principal investigator or study staff immediately if any serious adverse event occurs during the study period.

**Relationship to Study Products:** The clinician’s assessment of an AE’s relationship to test article (study drug) is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported. All AEs must have their relationship to study product assessed using the terms: associated or not associated. In a clinical trial, the study product must always be suspect. To help assess, the following guidelines are used.

**Associated:** The event is temporally related to the administration of the study product and no other etiology explains the event.

**Not Associated:** The event is temporally independent of study product and/or the event appears to be explained by another etiology.

**Serious Adverse Event (SAE):** An SAE is defined as an AE that meets one of the following conditions:

- a. Death during the period of protocol defined surveillance
- b. Life-threatening event (defined as a subject at immediate risk of death at the time of the event)
- c. An event requiring inpatient hospitalization or prolongation of existing hospitalization during the period of protocol defined surveillance
- d. Results in congenital anomaly or birth defect
- e. Results in a persistent or significant disability/incapacity
- f. Any other important medical event that may not result in death, be life threatening, or require hospitalization, may be considered a serious adverse experience when, based upon appropriate medical judgment, the event may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

**Hematological Investigations:**

Hematological investigations were performed at the times specified in the ‘Schedule of events’ as follows.
1. Complete blood count (CBC):
Hemoglobin, red blood cells (RBC), White blood cell (WBC) and ESR.

2. Blood chemistry:
Blood sugar, Bilirubin (Direct & Indirect), alkaline phosphates, SGOT, SGPT, creatinine, uric acid, total protein, albumin and globulin

3. Urine analysis:
Colour, specific gravity, pH, protein, glucose, ketones, bilirubin

Electro Cardiogram: ECG is helpful to assess the effect on cardiovascular system.

5. III. 3. Demographic Evaluation:
It is an invariable data, which is collected for having an idea of each subject about social and otherwise background. Individual assessment can be done considering the backdrop of the demographic data of each individual. Parents and home at this tender age play an important role in the psychological development of children. Hence the general information about parents was noted.

Details of the family members: Educated family members generally are believed to be more conscious about their children’s education. Education of father and mother was noted separate. The one who can read and sign is considered here as educated. There are few cases where a parent though illiterate, could sign. These cases were taken in to the category of illiterate.

Family Type: The child belongs to the category of Nuclear or Joint Family was noted.

Developmental History:
During Pregnancy:
The role of regular antenatal care which includes supplements (folic acid, iron, calcium etc) is well accepted for the brain development of the child. Hence the mothers of the children were asked about their ANC (whether Regular/ Irregular)
There are certain gestational conditions (Diabetes, Pre eclampsia etc) which require special medications during pregnancy which undoubtedly affect the baby. Hence, the H/O gestational conditions was asked and noted.
Tobacco/Misri addiction to the mother during pregnancy was also noted as this shows the harmful effect on overall development of the baby. Duration of Pregnancy, Birth weight, Labour type, any complications within 8 days after birth, presence of congenital anomaly are the important factors in the future development of the child. This information was also included in the Demographic part.

**Milestones:** According to pediatric science, certain age has been specified for achievement of various milestones. Milestones such as smiling, rolling over, and walking, speaking, self independency are the indicators of appropriate development of the child. Most of the Parents were unable to tell the exact age of milestones achieved so it was categorized as Early, average, Late, Never and don’t know.

Various diseases show the remittent over the body for longer period. In Demographic assessment, history of such diseases was asked along with the age at which it was occurred.

Apart from noting down the concerned history from parents, overall family history was considered under this heading. This provided a bigger platform in the understanding of the subject’s mentality. Certain diseases may transfer genetically to the next generation hence detailed family medical history was recorded.

Along with all this information, previous evaluations/treatments of psychiatric disease, psychological testing, neuropsychological diseases, learning disabilities, hearing/vision problems and current medication were also noted.

5. IV. Methodology:

Methodology followed is mentioned in two stages:
1. Screening & Recruitment period
2. Post Recruitment period

5. IV.1. **Screening & Recruitment period**

5. IV.1.A) Subject Screening Procedure (From June 09 to Oct.09):

- Since age limit for participation in project was 6-12 yrs., meetings
with teachers of 5th Std. (6 divisions) & 6th Std. of (6 divisions) of Modern Boys High school & Modern Girls high school & 3rd & 4th Std. (5 divisions each) of Modern Primary School were arranged separately for informing them about the project & explaining their role in this project.

- Teacher’s Questionnaires from total 22 teachers were procured for screening of slow learners.
- 400 students (out of approximately 1900 students) were screened as slow learner as per Teacher’s Questionnaire
- Parent meetings (three) were arranged in all three schools separately for the explanation of project.
- Parent’s Questionnaire & Informed consents were procured from parents.
- Out of 400 parents, 230 parents gave the voluntary consent.
- Students having age more than 13 years were excluded. 30 students had age more than 13 years

5. IV. 1. B) Psychiatric & Psychometric Evaluation ((From 26th July to 15th Dec.09):

- I.Q. assessments of 200 students were completed for screening.
- Psychiatric assessment of 200 students by consultant neuropsychiatrist was completed for determination of exclusion criteria.
- Adjustment Inventory assessment of 200 students was recorded
- Child Behavior checklist assessment of 200 students was procured from parents

5. IV.1. C) Physical Fitness evaluation (From 5th Dec.09 to 7th Dec.09):

- Thorough physical examination to rule out any major disorder by consultant physician of 180 students was completed.
- Laboratory testing for blood, urine & E.C.G. of 174 students was done for detection of any abnormality. 6 students denied laboratory investigation

5. IV. 1. D) Demographic assessment (From Aug. 09 to Dec.09):

- Demographic assessment of 180 students with the help of parents was done for socio demographic background evaluation & finding out any
cause for academic underperformance

5. IV. 1. E) Enrollment of Subjects & Procedure of randomization (From 7th Dec.09 to 21st Dec.09)

✓ Randomization: As per inclusion & exclusion criteria in protocol 171 subjects were enrolled in two groups ‘X’ & ‘Z’ as per random number allocation provided by consultant statistician.

Two groups were made:

i. Group X- 86 students in age group 6-13 years.

ii. Group Z- 85 students in age group 6-13 years.

<table>
<thead>
<tr>
<th>Group</th>
<th>Morning</th>
<th>Evening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Group</td>
<td>Capsule containing 68.18 mg of Shankhpushpi Ghana</td>
<td>Capsule containing 68.18 mg of Shankhpushpi Ghana</td>
</tr>
<tr>
<td>Control Group</td>
<td>Capsule containing 68.18 mg of Starch</td>
<td>Capsule containing 68.18 mg of Starch</td>
</tr>
</tbody>
</table>

✓ Baseline assessment of 171 students is recorded in C.R. F. before starting the Drug which includes:

i. Inclusion & exclusion criteria,

ii. Standardized Ayurvedic checklist in which each question had given rating 1, 2&3.

iii. Checklist for mental examination according to Ayurveda.

iv. Standardized checklist for medha pareeksha based on Mini Mental Status Examination for assessment of medha which contains examination of dhi, dhruuti, smruti, grahana, dharana, mano-buddhi indriya samyog, chintya & Sandnya dnyanam

v. General Ayurvedic examination with the help of Dashvidha & Ashtavidha pareeksha

vi. Examination of Vital signs i.e. pulse, B.P. Respiration, Height, body Weight & Abdominal girth
vii. Physical examination i.e. examination of general appearance of skin, ENT, Respiratory system, CVS, Neurological & abdominal system.

viii. Adverse Drug Reaction Form as per National Pharmacovigilance Program for ASU (Ayurveda, Siddha & Unani) drugs

✓ **Prior and Concomitant Therapy:**

All the parents were instructed to maintain strict compliance with the treatment. They were also instructed to avoid any other medications, including over the counter products without consulting the investigator, unless such medications were for emergency use. At each study visit, the investigator inquired parent/legal guardian about any medication(s) taken by the subject. Information of the same was recorded in the CRF with following details:

Drug name, dosage form, indication for use, total daily dose, route of administration, start and end date of the treatment.
Table 1: Schedule of Events. (Screening & Recruitment Period)

<table>
<thead>
<tr>
<th>Study Procedure</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>June 09</td>
</tr>
<tr>
<td>1. Subject Screening:</td>
<td>√</td>
</tr>
<tr>
<td>Selection of the school</td>
<td>√</td>
</tr>
<tr>
<td>Meeting with teachers</td>
<td>√</td>
</tr>
<tr>
<td>Teacher’s questionnaire</td>
<td>√</td>
</tr>
<tr>
<td>Preparation of drug dispensing &amp; accounting logs</td>
<td></td>
</tr>
<tr>
<td>Parent meeting</td>
<td>√</td>
</tr>
<tr>
<td>Parent’s questionnaire</td>
<td>√</td>
</tr>
<tr>
<td>ICF implementation</td>
<td>√</td>
</tr>
<tr>
<td>2. Psychiatric &amp; Psychometric Evaluation:</td>
<td>√</td>
</tr>
<tr>
<td>I.Q. assessment</td>
<td>√</td>
</tr>
<tr>
<td>Psychiatric assessment</td>
<td>√</td>
</tr>
<tr>
<td>AI assessment</td>
<td>√</td>
</tr>
<tr>
<td>CBCL from parents</td>
<td>√</td>
</tr>
<tr>
<td>Demographic assessment</td>
<td>√</td>
</tr>
<tr>
<td>Physical Fitness evaluation</td>
<td></td>
</tr>
<tr>
<td>Laboratory testing</td>
<td></td>
</tr>
<tr>
<td>3. Enrollment of Subjects &amp; Procedure of randomization</td>
<td></td>
</tr>
<tr>
<td>Randomization</td>
<td></td>
</tr>
<tr>
<td>Treatment Allocation</td>
<td></td>
</tr>
<tr>
<td>Baseline assessment</td>
<td></td>
</tr>
<tr>
<td>Prior and Concomitant Therapy</td>
<td></td>
</tr>
</tbody>
</table>
5. IV. 2. Post Recruitment Period:

5. IV. 2. A) Drug Dispensing & Accountability (From 21st Dec.09 to 20th Dec 10)
   - Dispensing of drug according to group was done at the interval of 15 days.
   - At the same time accountability of drug was also well maintained along with account of returned bottles.

5. IV. 2. B) Follow ups (From 21st Jan.2010 to 15th Jan 2011)
   - Mental examination as per Ayurveda
   - Medha pareeksha
   - General Ayurvedic examination, Vitals
   - Physical examination
   - Adverse Drug Reaction Form at the interval of one month is continued.

5. IV. 2. C) Parent’s Meeting :
2nd, 3rd & 4th meetings were arranged & Ayurvedic checklist was procured from parents at 90th, 180th day, follow up 9 & on 360th Day respectively.
5 IV. 2. D) Treatment Compliance

Every effort was made to encourage patient compliance with the dosage regimen and study protocol. Additionally, parent/legal guardians were informed to visit the study centre on scheduled dates. Those, who missed the scheduled visits, were informed telephonically to visit study centre within their timeline. In addition to this, teachers and students were organized to motivate parents and study subjects.

Every effort was made to encourage subject compliance with the study treatment as per protocol. The compliance to the treatment was assessed on the basis of adherence to visit schedule, drug accountability and other parameters deemed appropriate by the investigator. All patients were instructed to return their treatment, with any unused drug, to the investigator at each visit. A record of supplies dispensed, taken and returned was made in the CRF at the appropriate visit.

The detail methodology along with timeline is described in following tables…..
Table 2: Schedule of Events. (Post Recruitment for 1st 6 months)

<table>
<thead>
<tr>
<th>Study Procedure</th>
<th>Days and Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td>Dec 09</td>
</tr>
<tr>
<td>Dose dispensing</td>
<td>√</td>
</tr>
<tr>
<td>IQ</td>
<td>√</td>
</tr>
<tr>
<td>Adjustment Inventory</td>
<td></td>
</tr>
<tr>
<td>CBCL</td>
<td></td>
</tr>
<tr>
<td>Mental examination</td>
<td>√</td>
</tr>
<tr>
<td>Medha pareeksha</td>
<td>√</td>
</tr>
<tr>
<td>Ayurvedic examination</td>
<td>√</td>
</tr>
<tr>
<td>Vital Examination</td>
<td>√</td>
</tr>
<tr>
<td>Physical examination</td>
<td>√</td>
</tr>
<tr>
<td>Laboratory Investigation</td>
<td></td>
</tr>
<tr>
<td>Parent Meeting</td>
<td></td>
</tr>
<tr>
<td>Ayurvedic Checklist</td>
<td></td>
</tr>
<tr>
<td>Adverse Event</td>
<td>√</td>
</tr>
<tr>
<td>Serious Adverse Event</td>
<td>√</td>
</tr>
<tr>
<td>Concomitant Medication</td>
<td></td>
</tr>
</tbody>
</table>

Submitted by Centre for Post Graduate Studies & Research in Ayurveda, TAMV, Pune
Table 3: Schedule of Events. (Post Recruitment from 6months to 12 months)

<table>
<thead>
<tr>
<th>Study Procedure</th>
<th>Days &amp; Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FU7 July 10</td>
</tr>
<tr>
<td>Dose dispensing</td>
<td>√</td>
</tr>
<tr>
<td>Mental examination</td>
<td>√</td>
</tr>
<tr>
<td>Medha pareeksha</td>
<td>√</td>
</tr>
<tr>
<td>Ayurvedic examination</td>
<td>√</td>
</tr>
<tr>
<td>Vital Examination</td>
<td>√</td>
</tr>
<tr>
<td>Physical examination</td>
<td>√</td>
</tr>
<tr>
<td>AEs</td>
<td>√</td>
</tr>
<tr>
<td>SAEs</td>
<td>√</td>
</tr>
<tr>
<td>Concomitant Medication</td>
<td>√</td>
</tr>
<tr>
<td>Parent Meeting</td>
<td></td>
</tr>
<tr>
<td>Ayurvedic checklist</td>
<td></td>
</tr>
</tbody>
</table>
6. **Data Quality Assurance:**

To ensure accurate, complete and reliable data, the investigator maintained the records of IQ, CBCL, Adjustment Inventory score, MMS, Mental Examination as per Ayurveda, laboratory tests, ECGs, clinical notes, and patient’s medical records, in the patient’s file as original source document for the study.

All study data was then recorded on individual CRF implemented, used and maintained according to the ICH E6 guidelines. Qualified person monitored all aspects of the study carefully. Monitoring was conducted according to ICH-Good Clinical Practice (GCP) and in compliance with applicable regulatory guidelines.

7. **Statistical Methods Planned and Determination of Sample Size:**

The comparison is done mainly by ‘t’ test or parallel nonparametric test. The choice of ‘t’ test or the parallel nonparametric test depends on nature of variable under comparison. e.g. If the groups are independent ‘Two Independent Sample ‘t’ test’, ‘ Mann Whitney Independent Rank Sum Test’ are used. When these samples are paired ‘Paired ‘t’ test or Wilcoxon’s Signed Rank Test’ are used.

P value \( \leq 0.05 \) is considered statistically significant.

8. **Archives:**

The study was performed by Centre for Post Graduate Studies & Research in Ayurveda, Tilak Ayurved Mahavidyalaya, Pune and all data generated and recorded during this study will be stored in the Tilak Ayurved Mahavidyalaya’s Archives for five years.

9. **Protocol Deviation:**

No any deviation in Protocol.
10. Observations:

DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demography
No of female and male
Out of 171 subjects participated in the trial, number of female students was 60 (36%) & number of male students involved was 111 (64%)
Male to Female ratio was 2:1

Family type
Amongst the 171 subjects involved in the study, 123 (73%) subjects lived in Nuclear family & 46 (23%) subjects lived in Joint family.
Education:
Mother's Education

Amongst the parents of 171 subjects involved in the study, 6 (4%) mothers were graduated, 123 (72%) mothers had high school education, 17 (10%) mothers had primary education and 23 (14%) mothers were illiterate.

Father's Education

Amongst the parents of 171 subjects involved in the study, 12 (7%) fathers were graduated, 125 (74%) fathers had high school education, 20 (12%) fathers had primary education and 12 (7%) fathers were illiterate.
Ante natal care
Amongst 171 subjects, mothers of 158 subjects had taken the proper ANC & 11 mothers are without ANC

<table>
<thead>
<tr>
<th>Antenatal Care taken</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>93%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Habit/Addiction during pregnancy:
Amongst the 171 subjects involved in the trial, habbit of tobacco / Misri during pregnancy was found in mothers of 32 (19%) subjects & mothers of 137 subjects were without addiction.

<table>
<thead>
<tr>
<th>Usage of Tobacco/Misri during Pregnancy</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19%</td>
<td>81%</td>
</tr>
</tbody>
</table>
Special medications during pregnancy
Mothers of majority subjects (166 mothers i.e. 98%) had not taken any special drug other than antenatal care (e.g. antihypertensive, antiepileptic etc). Only 2% mothers were needed special drugs like antihypertensive.

Complication during pregnancy
Amongst 171 subjects, 147 mothers had complications like pre-eclampsia, infections, and toxemias during pregnancy.
Duration of Pregnancy
Mothers of majority subjects were completed full term of pregnancy (159), 2 subjects were born at 7th month, 5 subjects were born at 8th month & 3 subjects were post mature.

Labour Type:

Birth Weight
Most of the Parents (64%) were unaware about their child’s birth weight. Rest all students’ birth weight were within limit.

**Presence of Birth Defect, Feeding problems, Sleeping problems etc**

Majority subjects had absence of any birth defect (162 out of 171). Only 7 subjects had history of birth defects like cleft palate, feeding problems, sleeping problems etc.

**Birth Defect**

- Yes: 4%
- No: 96%

**Birth Presentation**

- Head: 97%
- Breech: 3%
Abnormality within 8 days after birth

Preponderance of participants did not show any abnormality within 8 days of after birth. Very few of them had Jaundice, Incubation, feeding problem and breathing problem. But they recovered soon from the mentioned defects.

History of past diseases
Almost 50% of participants had suffered from chicken pox and 33% from measles. In future there is a need to do epidemiological studies in this area.

Family History

![Bar chart showing family history diseases](image)

Alcoholism is seen to be the most important problem in these participants.

11.1 Adjustment for Covariates

Not applicable.

**11. STATISTICAL / ANALYTICAL ISSUES**

11.2 Handling of dropout or missing data

Dropout and missing data were handled by exclusion method.

11.3 Interim Analysis

No interim analysis was performed.

11.4 Multicoated Studies

Not applicable.
11.5 Multiple Comparisons
Not performed in this study

11.6 Use of “Efficacy subset” of subjects
IQ sub sets were studied and the detailed results are mentioned in the overall Results Part.

11.7 Active control studies intended to show equivalence
Not applicable

11.8 Examination of subgroups
Not applicable

11.9 Drug dose, drug concentration and relationships to response
Not applicable.

11.10 Drug-Drug and Drug disease interaction
Not applicable.

12.1 Extent of exposure:
Out of 171 subjects, 2 subjects are consent withdrawn before starting the drug. 86 subjects received placebo (Group ‘X’) in a dose of 1 ‘Cap’ twice a day for 12 months. Remaining 83 subjects received Cap Shankhapushpi (Group ‘Z’) in a dose of 1 ‘Cap’ twice a day for 12 months. From these, 71 subjects receiving placebo and 70 subjects receiving capsule Shankhapushpi completed treatment of 12 months.

12.2 Safety Analysis:
Annex XXII

12.3 DEATHS AND OTHER SERIOUS ADVERSE EVENTS:

12.3.1 DEATHS
No death was reported in the study.

12.3.2. OTHER SERIOUS ADVERSE EVENTS
No serious adverse event was reported in the study.

12.3.3. OTHER SIGNIFICANT ADVERSE EVENTS
No significant adverse event was reported in the study.

12.3.4. NARRATIVES OF SERIOUS ADVERSE EVENT
12.3.5. ANALYSIS AND DISCUSSION OF SERIOUS ADVERSE EVENT
Not applicable.

12.4 CLINICAL LABORATORY EVALUATION
Following investigations were conducted.

**Hematology**
There was no significant difference in the mean values of haematology parameters (hemoglobin, RBC count, WBC count and ESR) between treatment group (‘Z’) and placebo group (‘X’) with respect to experimental phase changes from baseline to the end of treatment. On analysis of individual clinical laboratory values, certain subjects in both treatment and placebo groups showed minor deviations in the values from the normal reference range, which were considered as clinically insignificant by the investigators as most of them were falling within acceptable percentage limit beyond normal reference range (Drug safety assessment in clinical trials. Edited by Gilbert GS. Marcel Dekker Inc. USA, pages: 222-223). The clinical laboratory values at 180\(^{th}\) Day & 360\(^{th}\) day were comparable to the baseline values.

**Biochemistry**
There was no significant difference in the mean values of biochemistry parameters (serum bilirubin, direct and indirect, alkaline phosphates, SGOT, STPT, blood sugar, blood urea, serum creatinine, total protein, albumin and globulin) between treatment group (Capsule C) and placebo group with respect to experimental phase changes from baseline to the end of treatment. Certain subjects in treatment and placebo groups showed minor deviations in the values from the normal reference range, which were considered as clinically insignificant by the investigators as most of them were falling within acceptable percentage limit beyond normal reference range (Drug safety assessment in clinical trials. Edited by Gilbert GS. Marcel Dekker Inc. USA, pages: 222-223). The clinical laboratory values at 180\(^{th}\) & 360\(^{th}\) day were comparable to the baseline values.

**Urine Analysis**
There was no significant change in the reported urine analysis parameters in treatment group (‘Z’) and placebo group (‘X’) with respect to experimental phase changes from baseline to the end of treatment.

**ECG Parameters**
Evaluation of ECG records before and after treatment with treatment group (‘Z’) showed that Capsule Shankhpushpi did not produce any serious adverse effects or any other changes that could affect the normal cardiovascular functions in comparison to the placebo group (‘X’).

12.5 VITAL SIGNS, PHYSICAL FINDINGS AND OTHER OBSERVATION RELATED TO SAFETY

**Pulse Rate**
There was no significant difference in the mean values of pulse rate between treatment
group and placebo groups. All the values were within normal reference range. Further, there was no clinically significant abnormality detected on within subject comparisons. No significant change was observed in vital parameters as well as safety parameters.

**Blood Pressure**
There was no significant difference in the mean values of systolic and diastolic blood pressures between treatment group and placebo group. All the values were within normal reference range. Further, there was no clinically significant abnormality detected on within subject comparisons.
Table 4: Details of evaluation

- Shankhpushpi Research Project
  - Experimental Work
    - Preparation of Latest review & Monograph of Shankhpushpi
    - Preparation & standardization of TQ, PQ, Demography, CRF, ADR and ICF and PIS in English & Marathi
    - Random Number allocation
  - Methodology
    - ICF execution
      - IQ, Psychiatric, Psychometric assessment
      - MMS, Mental, Physical Examination as per Ayurveda & Lab Investigations done
      - Drug dispensed at the interval of 15 days. Total 24 doses were dispensed
  - Preparation of Identical Capsules of Shankhpushpi & Placebo
  - Identification, Authentication & Standardization of Shankhpushpi
  - Preparation & Standardization of Shankhpushpi Ghana
  - Lab Investigations, IQ, Psychometric assessment at 180th & 360th Day
  - Follow up at every month (total 12 follow ups)
Table 5. Disposition of Subjects

<table>
<thead>
<tr>
<th>Screened (n = 400)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Informed Consent given by Parents (n = 230)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Demographic Assessment (n = 180)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Laboratory Investigations (n = 174)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Excluded (n = 50) Not meeting inclusion criteria</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Excluded (n = 6) Not willing for lab.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Day 0</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Enrolled &amp; Randomized (n = 171)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Excluded (n = 3) Lab Failed</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group X (n = 86)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Subjects completed (n = 86)</td>
</tr>
<tr>
<td>Lost to follow-up (n = 0)</td>
</tr>
<tr>
<td>Consent withdrawal – (n = 0)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group Z (n = 85)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Subjects completed (n = 81)</td>
</tr>
<tr>
<td>Lost to follow-up (n = 0)</td>
</tr>
<tr>
<td>Consent withdrawal – (n = 4)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Day 180</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Subjects completed (n = 75)</td>
</tr>
<tr>
<td>Lost to follow-up (n = 0)</td>
</tr>
<tr>
<td>Unwilling (n = 6)</td>
</tr>
<tr>
<td>Left school (n = 3)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Subjects completed (n = 76)</td>
</tr>
<tr>
<td>Lost to follow-up (n = 0)</td>
</tr>
<tr>
<td>Unwilling – (n = 4)</td>
</tr>
<tr>
<td>Left School (n = 1)</td>
</tr>
</tbody>
</table>
Subjects completed (n=75)
Lost to follow-up (n=0)
Unwilling– (n = 0)
Left school (n =0)

Subjects completed (n=73)
Lost to follow-up (n=0)
Unwilling– (n = 0)
Left school (n =0)

Subjects completed (n=72)
Lost to follow-up (n=0)
Unwilling– (n = 2)
Left school (n =1)

Subjects completed (n=71)
Lost to follow-up (n=0)
Unwilling – (n = 2)
Left school (n =0)

Subjects completed (n=72)
Lost to follow-up (n=0)
Unwilling– (n = 0)
Left school (n =0)

Subjects completed (n=70)
Lost to follow-up (n=0)
Unwilling – (n = 1)
Left school (n = 0)

Subjects completed (n=72)
Lost to follow-up (n=0)
Consent withdrawal – (n = 0)
Left school (n =0)

Subjects completed (n=69)
Lost to follow-up (n=1)
Consent withdrawal – (n = 0)
Left school (n =0)

Post drug Investigation

Subjects completed (n=67)
Absent for lab Investigation-(n=5)

Subjects completed (n=66)
Absent for lab Investigation-(n=3)
13. Final Results:

Evaluation of Ayurvedic Checklist:

Ayurvedic Checklist had been filled up by the parents on day 0-pre drug, day 90, day 180, and day 270\textsuperscript{th} and on 360\textsuperscript{th} Day that is end of the drug.

At Baseline the mean score for the group X is 30.6627(+/- 12.81) and Group Z is 31.5542 (+/- 12.51). As per the statistical evaluation, Pooled variance ‘t’ test, the P-value is \textbf{0.6479} (confirmed by Non-parametric Mann Whitney Independent Rank Sum Test, P-value=0.55949128). This shows (P-value) that at ‘baseline’ there is no difference in groups X & Z i.e. the groups are comparable with respect to Ayurvedic checklist scores.

Additionally the difference of mean scores of the day 0 and day 360 (Group X & Z) are compared. It is seen that the score reduction in group Z is more than group X. This is also statistically significant, P-value = \textbf{3.857E-06} which is also confirmed by Non-parametric Mann Whitney Independent Rank Sum Test, P-value=0.00000031).

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group X</td>
<td>30.66 ± 12.8</td>
<td>0.6479</td>
<td>NS</td>
<td>25.89 ± 10.02</td>
<td>(-5.7042 \pm 11.3318)</td>
<td>\textit{3.857 E-06}</td>
<td>HS</td>
</tr>
<tr>
<td>Group Z</td>
<td>31.55 ±12.51</td>
<td></td>
<td></td>
<td>17.16 ± 7.19</td>
<td>(-14.1857\pm9.4994)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Pooled variance ’t’ test is applied to compare Group X and Group Z scores**

**Evaluation of the Dharaniya Vega:**

The Dharaniya vega is assessed on day 0-Pre drug, day 90, day 180, 270th Day and on 360th Day that is at the end of the drug.

At Baseline the mean score for the group X is 11.2790 (+/-5.33) and Group Z is 11.3855 (+/-4.9233).

As per the statistical evaluation, Parametric Test-Pooled variance ’t’ test, the P-value is 0.8929 (confirmed by Non-parametric Mann Whitney Independent Rank Sum Test, P-value=0.72531082). This show (P-value) that at ‘baseline’ there is no difference in groups X & Z i.e. the groups are comparable with respect to Dharaniya Vega scores(Simple sum analysis). Additionally when the two groups are compared with weighted sum analysis, there
is no statistical significant difference into X & Z at baseline (P=0.9600) which is again confirmed by Non-parametric Mann Whitney Independent Rank Sum Test, P-value=0.79519404.

Additionally the difference of mean scores of the day 0 and day 360 (Group X & Z) are compared. It is seen that the score reduction in group Z is more than group X. This is also statistically significant by Simple sum as well as Weighted sum Analysis. P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.0012. (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.00233822) and P-value =0.0209 by weighted sum analysis (confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.01733578)

**Simple Sum Analysis**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group X</td>
<td>11.28±5.3</td>
<td>0.8929</td>
<td>NS</td>
<td>8.98±4.03</td>
<td>-2.6 ± 4.9</td>
<td>0.0012</td>
<td>HS</td>
</tr>
<tr>
<td>Group Z</td>
<td>11.38±4.9</td>
<td></td>
<td></td>
<td>6.08±3.26</td>
<td>-5.1±4.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Weighted Sum Analysis**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group X</td>
<td>25.58±15.8</td>
<td>0.9600</td>
<td>NS</td>
<td>16.94±10.63</td>
<td>-9.2 ± 14.65</td>
<td>0.0209</td>
<td>HS</td>
</tr>
<tr>
<td>Group Z</td>
<td>25.7±14.5</td>
<td></td>
<td></td>
<td>10.28±8.02</td>
<td>-14.58 ± 12.65</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dharaniya Vega**

![Dharaniya Vega Graph](image-url)
Evaluation of Mental Examination as per Ayurveda:

As per the guidelines of ayurveda, Mental Examination is assessed at the interval of one month. When the baseline scores of both the groups are compared, there is no statistical significant difference, P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.9269 (confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.38971346).

Furthermore, when the weighted Sum analysis is done, statistical significance is not seen in both the groups with respect to the baseline scores. P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.6675 (confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.68810285)

Then the mean scores of 360th Day in both the groups are also compared statistically and it is seen statistically non significant in Simple sum as well as Weighted Sum analysis.

**Simple Sum Analysis:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.2016 (Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.00001160)
**Weighted Sum Analysis:** P-value obtained by Parametric Pooled Variance ‘t’Test = 0.1651 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.15956555). Details are shown in the following table:

### Simple Sum Analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of Difference from Baseline</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group X</td>
<td>2.13±2.9</td>
<td>0.9269</td>
<td>NS</td>
<td>0.4054±1.423</td>
<td>-1.6081±2.5201</td>
<td>0.7397</td>
<td>NS</td>
</tr>
<tr>
<td>Group Z</td>
<td>2.09±3.2</td>
<td>0.1594±0.74</td>
<td>-1.7536±2.7084</td>
<td>0.7397</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Weighted Sum Analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of Difference from Baseline</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group X</td>
<td>3.79±6.73</td>
<td>0.5945±2.5903</td>
<td>-2.9594±5.8577</td>
<td>0.4299</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group Z</td>
<td>4.27±7.92</td>
<td>0.1527±0.7250</td>
<td>-3.8333±7.4114</td>
<td>0.4299</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

When the difference in mean scores of final day and baseline are compared, it is seen that those scores are also statistical not significant.

**Simple Sum Analysis:** P-value obtained by Parametric Pooled Variance ‘t’Test = 0.7397 (Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.94065792)
**Weighted Sum Analysis:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.4299 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.77180639)

---

**Evaluation of MINI MENTAL SCALE Examination:**
Mini Mental Scale Examination is assessed at every month. The Baseline scores of both the groups are found statistically non-significant. P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.6873 (Confirmed by Nonparametric Mann Whitney Independent Rank Sum Test P-value=0.81174042)

There is significant difference when the difference in mean scores of final day and baseline are compared, P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.00000003190. (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.0000003)

---

**MINI MENTAL SCALE Score**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline P Value</th>
<th>Signi Level</th>
<th>Final Mean</th>
<th>Difference in Mean</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>27.4186 ± 3.6765</td>
<td>0.6873 NS</td>
<td>29.7183 ± 3.1766</td>
<td>2.3239±3.5285</td>
<td>0.00000003190 HS</td>
<td></td>
</tr>
<tr>
<td>Gr.Z</td>
<td>27.1566 ± 4.7227</td>
<td></td>
<td>33.7714 ± 2.8699</td>
<td>6.3142±4.0055</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evaluation of Adjustment Inventory Examination:

Adjustment Inventory scale was assessed on baseline, 180th day and 360th day. In-group X, mean Adjustment Inventory score was 31.7441 at baseline. Corresponding finding in-group Z was 32.5744. When these mean scores evaluated statistically, they are found non-significant.

Additionally when the difference in the mean score of Post & Baseline AI score is compared, there is a significant difference found. (P=0.0030). The details are given in the following table:

### Adjustment Inventory Score

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>31.7441 ± 6.7478</td>
<td>0.4006</td>
<td>NS</td>
<td>88.4142 ± 7.1092</td>
<td>2.5352 ± 8.5854</td>
<td>0.0030</td>
<td>HS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>32.5744 ± 7.4166</td>
<td></td>
<td></td>
<td>90.6204 ± 7.8721</td>
<td>6.7428 ± 7.9375</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evaluation of IQ examination:
Intelligent Quotient of each student was assessed at 0 day, 180th Day and 360th day. The IQ score is based on the Verbal, Performance & total IQ.

**Verbal IQ**
When the Baseline and Final Verbal IQ scores from both the groups (Group X & Group Z) were examined statistically, at baseline, it is found non-significant. The P-value obtained by Parametric Pooled Variance ‘t’ Test is 0.6458. (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.67687912).
And when the difference in mean score of Final Visit- Baseline compared, P-value obtained by Parametric Pooled Variance ‘t’Test = 0.4329 (confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.46070288)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>80.6923±12.9626</td>
<td>0.6458</td>
<td>NS</td>
<td>84.5598±8.3799</td>
<td>3.3208±12.7085</td>
<td>0.4329</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>81.6681±14.5725</td>
<td></td>
<td></td>
<td>85.9589±8.3111</td>
<td>5.0236±12.9115</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Verbal IQ**

**Verbal IQ (BT: AT)**

![Bar chart showing Verbal IQ scores for Groups X and Z.]

**Difference in Mean (Performance IQ)**

![Bar chart showing the difference in mean performance IQ scores for Groups X and Z.]

Submitted by Centre for Post Graduate Studies & Research in Ayurveda, TAMV, Pune
**Performance IQ**

Same as that the performance IQ scores at Baseline (Mean score of Group X: 86.6979 & Group Z: 88.0209) when compared, found statistically non-significant. The P-value obtained by Parametric Pooled Variance ‘t’ Test is 0.3479. (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.3022911). And when the difference in mean score of Final Visit- Baseline compared, Final Visit- Baseline: P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.3447 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.55956094)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>86.6979± 8.2189</td>
<td>0.3479</td>
<td>NS</td>
<td>92.2685±9.8501</td>
<td>5.5368± 9.2557</td>
<td>0.3447</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>88.0209± 9.9989</td>
<td></td>
<td></td>
<td>95.2820±10.4290</td>
<td>7.2528±11.9864</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Performance IQ**

![Performance IQ Graph](image-url)
Additionally when the Average IQ scores of Baseline and Final visits (both the groups) were compared, unfortunate to found statistical significant. P-value obtained by Parametric Pooled Variance ‘t’Test at baseline is 0.3991. (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.57241295)

In the next comparison, the difference in the mean (both the groups) obtained Final day-Baseline was considered

**Final Visit- Baseline:** P-value obtained by Parametric Pooled Variance ‘t’Test = 0.2614 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.37023687)
Average IQ

**Evaluation of Child Behavior Checklist Examination:**

The CBCL forms are filled up by the parents on three intervals, 0 day, 180th Day and on 360th day. The information is considered in four parts, Internal, External, and Total & Competent.

**Internal**

In the beginning, the findings obtained for CBCL score at Baseline & final visit were compared in both the groups. They are found statistically not significant at baseline and at final visit. The details can be seen in the following table.
**Baseline:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.4558 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value = 0.33468576)

When the Difference of mean score of baseline & final are compared, p-value obtained is 0.8129, which is statistically non significant.

**Final-Baseline:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.8129 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value = 0.75359563)

### Internal CBCL

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>62.1627±11.0845</td>
<td>0.4558</td>
<td>NS</td>
<td>37.7313±6.7455</td>
<td>-24.6716±12.2664</td>
<td>0.8129</td>
<td>NS</td>
</tr>
</tbody>
</table>

---

![CBCL Internal (BT:AT)](image)

![Difference in Mean (Internal)](image)
External CBCL

External: Baseline: P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.2919
(Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.64368147)

When the mean scores of difference of scores of final- baseline are compared, p-value obtained by Parametric Pooled Variance ‘t’ Test = 0.6115 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.88670124), which is not significant

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of Difference from Baseline</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>61.6627±12.7994</td>
<td>0.2919</td>
<td>NS</td>
<td>57.0895±8.7068</td>
<td>-4.5373±16.4963</td>
<td>0.6115</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>63.5060±9.5717</td>
<td></td>
<td></td>
<td>57.5970±8.8301</td>
<td>-5.7761±11.1624</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![External (BT:AT) Mean Score Graph](image)
**Total CBCL**

**Baseline:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.2582 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.56469163)

When difference of mean scores of Final and Baseline are compared, they also found statistically non-significant. Final-Baseline: P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.2919 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test-value=0.35321153)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>62.6162±9.7680</td>
<td>0.2582</td>
<td>NS</td>
<td>60.4626±10.5806</td>
<td>-2.6716±13.1487</td>
<td>0.2919</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>70.2650±61.7386</td>
<td></td>
<td></td>
<td>59.7761±10.1321</td>
<td>-11.8507±69.7748</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Competent

**Baseline:** P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.6771 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.99371823)

When difference of mean scores of Final and Baseline are compared, they also found statistically non-significant. Final- Baseline: P-value obtained by Parametric Pooled Variance ‘t’ Test = 0.5718 (Confirmed by Non Parametric Mann Whitney Independent Rank Sum Test, P-value=0.75866018)
<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>P Value</th>
<th>Signi Level</th>
<th>Final</th>
<th>Difference in Mean (Final-Baseline)</th>
<th>P-value of (Difference from Baseline)</th>
<th>Signi Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr.X</td>
<td>33.1395±9.7475</td>
<td>0.6771</td>
<td>NS</td>
<td>59.0149±10.3798</td>
<td>25.5074±14.2045</td>
<td>0.5718</td>
<td>NS</td>
</tr>
<tr>
<td>Gr.Z</td>
<td>32.5542±8.4236</td>
<td></td>
<td></td>
<td>58.8955±8.8952</td>
<td>26.7611±11.2291</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Competent CBCL (BT:AT)

- **Group X**
  - Baseline: Score ±
  - Final: Score ±

- **Group Z**
  - Baseline: Score ±
  - Final: Score ±

### Difference in Mean (Competence)

- **Group X**
  - Mid-Baseline: Difference
  - Final-Mid: Difference
  - Final-Baseline: Difference

- **Group Z**
  - Mid-Baseline: Difference
  - Final-Mid: Difference
  - Final-Baseline: Difference
“Intellect” directly relates the futuristic carrier and reflects in the form of learning skills. The substandard levels of learning skills (slow learning) i.e. relatively hampered reading, writing & mathematical are present in 8% of school going children. Keeping this in mind, the study has been designed to assess the efficacy and safety of Shankhapushpi in slow learners of age group 6-13 years and to evaluate Nootropic effect of Shankhapushpi Ghana as a Medhya Rasayana.

To achieve this aim, certain assessment tools were taken into consideration.

- Ayurvedic Checklist
- Dharaniya Vega
- Mental Examination as per Ayurveda
- Mini Mental Scale Examination
- Adjustment Inventory Scale
- Intelligent Quotient
- Child Behaviour Checklist

Above are the assessment tools to reach to the ultimate goal.

AYURVEDIC CHECKLIST:

Ayurvedic Checklist is the evaluation form which was filled up by the parents on regular intervals. Various evaluation points according to Ayurveda were considered. Qualitative analysis was made based upon the information given by the parents. Total score was taken at the end.

Ayurved Checklist is basically to check the behavioral pattern seen in humans (especially younger children). Questions are arranged as per ascending integrity (Mild, Moderate, and Severe scored as 1, 2, 3)

This includes: “Anavasthitatva” i.e. Mental as well as physical unsteadiness, “Lobha”: (Perplexity Greed), “Bhaya” (Fear), “Krodha” (control over anger), “Mohá” (Passionate about), “Akasmát rodana” (Grief), “Aupadhikatva” (nastiness), “Aalasyá” (Laziness), “Satva” (tolerate mental as well as Physical harm) etc.
Parents were counseled regarding this Questionnaire. Aim of this medication is to reduce the score.

As per the results obtained at Initial Visit and Final visit, the score reduction was seen in both the groups but the reduction percentage in the study group i.e. the group which consumed ‘Shakhapushpi’ tablets was far more than the placebo group (P-value=3.857 E-06) This shows Shankhapushpi is immensely effective in changing the behavioral pattern in the slow learners. This might be due to reduction in spontaneous motor activity, reduction in exploratory behavioral pattern, and suppression of aggressive behaviour. (Subhangi A. Pawar et al)\textsuperscript{12}

**DHARANIYA VEGA: (Emotions to be controlled)**

According to Ayurveda one should control the urges of greed, envy, and jealousy, love (desire) etc & gain control over his sense organs for prevention of onset of psychological disorders. In this study these urges (Dharniya Vega) are assessed to check the control over emotions. One can control emotions only when mind is stable. Following points were taken into consideration.

\begin{itemize}
  \item **Lobha:** Perplexity Greed \hspace{2cm} **Krodha:** Irsha:
  \item **Shoka:** Grief \hspace{2cm} **Maan:** Atiraga:
  \item **Bhaya:** \hspace{2cm} **Nirlajjata:** Abhidhya:
\end{itemize}

As same as that of Ayurvedic Checklist these points were assessed as Not Present, Mild, Moderate and severe (score as 0,1,2,3 respectively). Intention was to see the reduction in the score from pre to final visit score.

According to the results, initially both groups show almost same mean of scores which indicates that both groups are at same level. Finally there is reduction of scores in both groups, but in placebo group reduction is not significant. In study group reduction in final score is more which is statistically significant (P-value=0.0012).This might be due to It nootropic as well as psychotropic effect of ‘Shankhapushpi.’ (A K Mehta)\textsuperscript{13}

These results indicate that Shankhapushpi enhances the power of mind control which is helpful to achieve the specific goal.
MENTAL EXAMINATION AS PER AYURVEDA

Ayurveda has its own principles & ways to oversee these principles. In Ayurveda detail methods for examination of mind are time-honored. Based on these principles & methods in present study mental examination as per Ayurveda was carried out at certain intervals. Intention to carry this examination is to rule out any mental abnormality. This includes assessment of ladders of thought process

Chintya (-to be thought about)
Vicharya (Questionable/to be discussed)
Oohya (Speculation)
Dhyeya (-Objectives)
Sankalpa (-to determine)

These steps are critically reviewed as Samyak (Normal), Ayoga (Negative), Mithyayoga (Perverted), and Atiyoga (Excessive). Each step is further assessed as per grades (Mild, Moderate and Severe)

As per inclusion criteria all the participants enrolled were physically & mentally healthy. As per results, at baseline scores of both groups are nearly in same range. When we compared the baseline & Final scores, there is no significant difference in both groups (P-value=0.7397).

MINI MENTAL SCALE EXAMINATION:

Mini Mental Status Examination

With the assistance of this scale it is possible to observe the following abilities of the participants.

Writing, Copying, Repetition, Immediate recall, Naming, Delayed verbal call, Attention, 3-stage command, Orientation of time, Orientation to place.

One complex sentence was asked to write. Initially most of the Subjects could not write the full corrected sentence. But after some period till last visit, consistent improvement was seen in both the groups. Although the improvement seen in study group was far better than the placebo group.

The participants were asked to copy the Interlocking pentagons. At the beginning most of the participants can not copy the shape properly. Subsequently participants could copy the shape properly. In Study group, the progress was more than the placebo.
It is observed that the factors like Repetition, Immediate recall, Naming are depend on the concentration of the participant. Many times it was observed that if the participant was at ease, then the score obtained was better and when he/she was in a hurry (due to any reason like eager to attend PT hour, drawing class, and short recess etc), the reflection could be seen on the answers and ultimately on the score. Situation was same for both the groups still improvement in study group is more than placebo. In case of assessment of Orientation of time & Orientation to place, there were many factors which can affect the answers e.g. if student was asked today’s date & if the day was special for that particular student like his birthday, he/she can easily reproduce the correct answer. Next follow up he/she may give the wrong answer for the same question. These affecting factors are same for both the groups. Still at the end, study group shows statistically significant improvement in the performance.

Certainly, a practice effect for this test is observed but it is present in both groups, hence nullified. Considering all these facts, we can conclude that improvement in study group is more than placebo group which is also statistically significant (P-value = 0.00000003190). This might be due to cognition enhancing effect of ‘Shankhapushpi’ (Nahata et al)\textsuperscript{14}

**INTELLIGENT QUOTIENT:**

For this Wechsler’s I.Q. test (Indian Adoption) is used. The original WISC as well as its Indian adaptation works on the Point Scale and all items of a given type are grouped together and arranged in increasing order of difficulty

IQ was assessed in two categories, Verbal & Performance. Verbal IQ includes Information test, General comprehension test, Arithmetic test, Analogies and Similarities, Vocabulary test, Digit span test. In Present study, more improvement is observed in study group as compared to placebo group although this improvement is not statistically significant. (P-value of difference from baseline = 0.4329) This might be because of following observations:
Verbal IQ score mainly depends on surrounding environment. Affirmative surrounding plays important role in expansion of vocabulary, general knowledge etc. As per demographic assessment in the present study, most of the subjects were from low socioeconomic background. Parents of majority subjects had just completed their primary education & working on daily wages. Almost all the subjects reside in slum areas. Characteristics related to family structure and resources: single parents, parents with low educational levels and low literary scores, unemployed parents and young parents definitely shows inverse effect on Intelligence development. The above picture suggests that the surrounding environment regarding theses subjects was not very much encouraging in overall intellectual development of the child which might not helpful for increase in score of verbal IQ. (Christiane capron et al) As these parents are from such low socio-economic background & are working on daily wages, thus not able to provide their valuable time with their kids. It is seen that the parents who interact frequently with their children, make numerous learning and reading materials available, encourage the development of new skills, use complex sentence structures in conversation, and so on—are associated with higher IQ scores in children.

Performance score depends mainly on concentration, speed & accuracy. Inattentive and hyperactive child may be compromised in score and it definitely will reflect in the IQ scores. As per observations from present study, majority of participants were not much willing to attend classes during school time. Percentage of absence was more. Additionally, most of the time they were physically present in the class and very much passionate about their recess and classes like Physical Training where they used to spend time in playing or other unproductive activities. As per Research, school attendance is very much useful in child’s proper development. One probable reason why school attendance affects IQ is that it encourages acquisition of more advanced cognitive processes—rehearsal, organization, metacognition. School provides a systematic means through which children can acquire many concepts and perspectives those previous generations have developed to tackle day-to-day tasks and problems effectively. Having brought the attentiveness and having settled the hyperactive child may lead us to his/her ‘original’ IQ, which is higher than the previously hyperactive and inattentive child. In present study it is clinically observed that there is more improvement in
performance scale than the verbal scale although it is not statistically significant (P-value of difference from baseline = 0.3447). This might be increased attentiveness due to ‘Shankhapushpi’.

Average IQ stands for mean of verbal & performance scale. Improvement is observed in both the groups but it is more in study group than the placebo group. As the age increases, there may be a change in IQ score might be due to maturity. In present study the time between pre & post Assessment was 12 months. Hence improvement is seen in both the groups. However there is more improvement in study group. (P-value of difference from baseline =0.2614)

**C.0hild Behavior Checklist (CBCL) : (Assessing violent behavior and related construct in children and Adolescents)**

This assessment was categorized in internal, external, total & competent scales. The main issue in assessing the CBCL was the presence of Parents. As discussed above; Most of the parents were working on daily wages. Ethically and principally, CBCL must be assessed by the same parent at each visit. Considering the socio-economic background of these subjects it was not possible to force the same parent to be present at each and every assessment of CBCL. Certainly there was a substantial difference in view of mothers and fathers regarding their child. In many cases CBCL was filled by close relatives like grandparents, elder siblings etc. Considering all these facts, it was not feasible to acquire promising results. Improvement can be seen in Internal (P-value=0.8129), External (P-value=0.6115), Total score (P-value=0.2919) as well as Competent CBCL (P-value=0.5718), although it is not statistically significant. This clinical improvement might be reduction in exploratory behavioral pattern, and suppression of aggressive behavior due to ‘Shankhapushpi’. (Subhangi A. Pawar et al)\(^{19}\)

**Adjustment Inventory for school going children (By Jnana Prabodhini’s Institute of Psychology, Pune)**

As per the Principals of Adjustment Inventory, Majority of the times it is seen that the high scorer students are well adapted with the school environment. They like their teachers, enjoy school life, are happy with their schoolmates & feel that the school is conducted
systematically & fairly. The poorly adapted students with low scores dislike their teachers, have complaints about school life & schoolmates & feel that they get an unfair treatment in the school. They may express a desire to withdraw from school. Present study was carried out in such slow learners with poor performance in their academia. So the main aim of this test was to see the score improvement. As per the obtained results the score improvement was seen in both groups but statistically significant improved score was observed in study group (P value=0.0030). This shows that “Shankhapsuhpi” improves the adaptation capacity in children.

15.0 REFERENCES


4. Sharma K, Bhatnagar M, Kulkarni SK, Source: B.N. PG College of Pharmacy, Udaipur 313 001, India.)


10. Effect of Convolvulus pluricaulis Choisy. on learning behaviour and memory enhancement activity in rodents, Nahata, Alok; Patil, U. K.; Dixit, V. K.


16. Assessment of effects of socio-economic status on IQ in a full cross-fostering study, CHRISTIANE CAPRON & MICHEL DUYME, Laboratoire Génétique, Neurogénétique et Comportement, URA 1294, CNRS, UFR Biomédicale, Université Paris V, 45 rue des Saints-Pères, 75720 Paris Cédex 06, France.


Annexure I

Standardization of Shankhapushpi
**Certificate of Analysis**

Product name : Shankhapospi Extract  
Batch No : NBF/9059  
Mfg date : Nov 09  
Exp. Date : Oct. 12

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>TESTS</th>
<th>SPECIFICATION</th>
<th>RESULT</th>
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<tbody>
<tr>
<td>1.</td>
<td>Description</td>
<td>Blackish brown color</td>
<td>Passes</td>
</tr>
<tr>
<td>2.</td>
<td>Total Ash Content</td>
<td>Not More Than 17 %</td>
<td>16.30</td>
</tr>
<tr>
<td>3.</td>
<td>Acid insoluble ash</td>
<td>Not More Than 8 %</td>
<td>7.81</td>
</tr>
<tr>
<td>4.</td>
<td>pH of 5% solution</td>
<td>4.0 – 7.0</td>
<td>5.33</td>
</tr>
<tr>
<td>5.</td>
<td>Alcohol soluble Extractive</td>
<td>Not Less Than 6 %</td>
<td>11.98</td>
</tr>
<tr>
<td>6.</td>
<td>Water soluble Extractive</td>
<td>Not Less Than 10 %</td>
<td>12.68</td>
</tr>
<tr>
<td>7.</td>
<td>Tapped bulk density</td>
<td>0.2 - 0.8</td>
<td>0.67</td>
</tr>
<tr>
<td>8.</td>
<td><strong>Microbial Test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8a.</td>
<td>Total plate count</td>
<td>Not More Than 10000 cfu/g</td>
<td>110</td>
</tr>
<tr>
<td>8b.</td>
<td>Yeast &amp; Moulds</td>
<td>Not More Than 100 fs/g</td>
<td>30</td>
</tr>
<tr>
<td>8c.</td>
<td>E.Coli</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>8d.</td>
<td>Salmonella Species</td>
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<td>Absent</td>
</tr>
<tr>
<td>9</td>
<td><strong>Assay</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Shankhapospi extract</td>
<td>TLC for scopoletin</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Remarks: The above referred batch conforms to the specification of Shankhapospi extract with respect to the above mentioned tests.

Nitin Jadhav  
Quality control  
Nisarga Biotech Pvt. Ltd  

Email: krushitek@vsnl.com
T.L.C (Thin Layer Chromatography)

Common name : Sankhapuspi
Botanical name : Convolvulus microphyllus
Marker compounds : Scopoletin

T.L.C Plate :

Result : spots glowing in UV light – wave length-377nm
8:D. Trial Design

8:D.1. The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. Description of trial design –

- **Primary end point:**
  1. Change from baseline in scholastic performance.
  2. Improvement in reading, writing & mathematical skill as shown in linguistic, mathematical, motor, social and behavioral performance, etc.

- **Secondary end point:**
  1. To assess the improvement in mental status of the patients as per Ayurvedic Guidelines.
  2. Change from baseline in IQ, verbal and performance scale.
  3. Change from baseline in child behavior profile.
  4. Change from baseline in social adjustment.

- **Safety end point**
  1. Change in baseline investigations
  2. Change from baseline in side effects rating

8:D. (2.) A description of the type / design of trial to be conducted (e.g. double blind, placebo controlled, parallel design) and a schematic diagram of trials design, procedures and stages.

- Prospective.
- Double blind.
- Placebo controlled.
- Parallel design.

SCHEMATIC DIAGRAM OF TRIAL DESIGN, PROCEDURES AND STAGES

```
Medicine preparation
  ↓
Permission from IEC
  ↓
Permission from the head of the institute
  ↓
Screening of all the classes
```
Feed back from teachers
(For screening of Slow learners based on last two years progress report and specially prepared questionnaire)

Parent meeting and counseling

Filling of informed consent form
Inclusion of students as per the inclusion criteria

Health check up -Medical evaluation
Psychometry (IQ test, CBCL, adjustment inventory)

Group A- (Study group)    Group B (Control Group)

24 follow-ups
(Follow up of both groups for 1 academic year)

Events and time schedule

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Safety Parameter</td>
<td></td>
</tr>
<tr>
<td>Hematology</td>
<td>✓</td>
</tr>
<tr>
<td>Chemical</td>
<td>✓</td>
</tr>
<tr>
<td>Efficacy parameter</td>
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</tr>
</tbody>
</table>
Clinical | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔
Psychometric | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔
Biochemical | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔

Recording Observations (Data Management)

After treatment analysis

Conclusion

Procedure

1. Based upon last two-year scholastic performance, children labeled, as slow learners will be recruited in the present study.
2. A informed consent from the head of the institution, parents and ethical committee will be taken at the outset. The investigator is responsible for the appropriate conducting and documenting informed consent sheet from every patient entering the study on the approved consent form. A copy of then signed consent form will be given to the teacher and the parents. Annex B
3. A Proforma will be prepared incorporating signs and symptoms & psychiatric evaluation for slow learners. CRF-Annex A

Details of evaluation

➢ Socio demographic background information
  • Students name.
  • Fathers /Guardians name.
  • Address.
  • Family religion and cast.
  • Family type.
  • Number of family members.
  • Particulars of family members – age, gender, marital status, education, occupation, income etc.

➢ Medical history (from parents).
  • Full term normal delivery or not.
  • Child’s health in past year: good /fair / unwell.
  • H/O head injury /epilepsy, any systemic disease, infectious disorder.
  • Any current medication.
  • Any Significant family history.

➢ Thorough mental and physical status evaluation will be done (including Dashavidha and Ashtavidha Pariksha and
Examination of Dhi, Dhruti, Smruti) Medical and Psychiatric evaluation will be done (Psychiatric evaluation as per DCR, ICD 10, WHO).

➢ Scholastic performance of last 2 years will be seen.

4. These students will be screened by IQ test and Psychometric scales.

5. Their behavior profile and adjustment will be documented.

6. Baseline lab investigation as well as side effect scale will be applied. Proforma for pharmacovigilance (ADR Record) will be applied.

7. Children will be allocated randomly in two groups.

8. Groups –

   Two groups will be made
   1) Study group – 80 students in age group 6-13 years.
   2) Control group- 80 students in age group 6-13 years.

<table>
<thead>
<tr>
<th>Group</th>
<th>Morning</th>
<th>68.18 mg S.G.Tab</th>
<th>68.18 mg SG tab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>/or equivalent churna</td>
<td>/or equivalent churna</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>68.18 mg starch</td>
<td>68.18 mg starch</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

However dosage variation study will be conducted in different dose level such as 200, 600 and 800 mg of churna in 7 cases each for a period of 1 month. Maximum effective dose will be considered as dose of trial drug.

9. Side effect scale will be applied -

   I\textsuperscript{st} After 15 days
   II\textsuperscript{nd} After 30 days
   III\textsuperscript{rd} After 90 days
   IV\textsuperscript{th} After 180 days
   V\textsuperscript{th} After 9 Months
   VI\textsuperscript{th} After 12 Months

10. Lab at entry and exit.
Annexure XI

Inclusion Exclusion Criteria
Subject Selection Criteria

Inclusion Criteria: -
- Children admitted in the school, children of age group. 6 to 13 years of either sex.
- Children screened as slow learners as per clinical examination.
- Consistent academic underperformance – last 2 year or more years.
- Consenting parents.

Exclusion criteria: -
- Any past or present psychotic symptoms.
- IQ below 70 (mentally retarded or subnormal children.).
- Past head injury warranting hospitalization.
- Any major medical illness.
- Congenital anomalies like Down syndrome.
- Uncorrectable sensory handicap.
- Current antiepileptic medication.
- The patients who have used any other investigation drug one month prior to start of study treatment.
- Use of any other immunomodulatory drug one month prior to start of study treatment

Subject withdrawal criteria: -
- Patient wishes to discontinue the treatment during trial treatment.
- Patient has lost 2 follow up for 2 consecutive visits.
- Serious adverse reaction and stage 3 toxicity is developed.
- Patients who are withdrawn subjects will be followed same as the treatment groups.

Note – The withdrawal patients will be replaced by having fulfilled criteria of inclusion and follow up thereafter.