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# AN EXPERIMENTAL STUDY TO EVALUATE THE EFFICACY OF GUDUCHYADI NIRUHA BASTI IN THE MANAGEMENT OF PARKINSONISM

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## ABSTRACT

Parkinsonism is typically considered a chronic progressive neuro-degenerative movement disorder. In the recent times it was seen that Constipation is an early indicator and a common symptom which might be a possible cause for Parkinsonism. This disease is explained as syndrome comprising of various groups of disorders that can be attributed to Parkinsonism. One of the very important concepts quoted in Ayurveda is the Concept of avarana, where the gati, the unique feature of Vata is obstructed by Kapha dosha, thus leading to the disease. The best modality for such a disease condition explained by our Acharyas is the Basti chikitsa. Very few experimental studies have been taken up, on Basti karma to provide the data proving the efficacy of this clinically effective procedure. Hence to give preclinical support to the effectiveness of Guduchyadi niruha basti explained in the classics, this experimental study was selected. For this a battery of well-known Neuro-muscular tests were selected with main focus on the efficacy in test protocols supposed to be predictive for the efficacy in treatment of Parkinsonism namely, Rota rod apparatus, Oxotremorine Test, Anti-Reserpine Test, L-Dopa Potentiation Test. Significant reversal of symptoms was seen in this work. Therefore from the data harvested from animal experimentation, it can be concluded that there is definite activity of Guduchyadi Niruha Basti in the effective management of Parkinsonism.

**KEYWORDS:** Parkinsonism, Guduchyadi Niruha Basti, Wister Albino Rats, Anti-parkinsonian activity.

## MATERIALS AND METHODS

Healthy Wister albino rats were obtained from the animal house attached to the department of Pharmacology & Toxicology of SDM Centre for research in Ayurveda and Allied Sciences Udupi, India and maintained at (temperature at 25 to 27$^{o}$C, humidity of 50 to 55% and 12 hr light and dark cycles). Healthy Wister albino rats of either sex weighing about 150 -200 gm were selected and divided into 4 groups. The selected animals were maintained properly under the prevailing husbandry conditions. They were marked over the Head, Neck, Body, Tail, Forelimb and No mark for easy identification in each group. They were fed with Champak feeds and Foods brand rat pellets feed and water ad libitum.

**Table no: 1 Animal grouping**

| Sr. No. | Group | Treatment | No of animals |
|---|---|---|---|
| 1. | Normal control | No treatment (maintained with normal rat feed and water ad libtum) | 6 |
| 2. | Reference standard | Test specific drugs | 6 |
| 3. | Guduchyadi Niruha Basti group 1 (GNB 1) | Drug basti | 6 |
| 4. | Guduchyadi Niruha Basti group 2 (GNB 2) | Drug basti higher dose | 6 |

### Test Drug Preparation

The Niruha Basti was selected from the Sushruta Samhita Chikitsasthana.[1] Chapter 38$^{th}$ and as the major active ingredient was Guduchi it was named Guduchyadi Niruha basti. Raw drugs were obtained from the S.D.M Pharmacy, Kuthpady, Udupi and Basti was freshly prepared daily in the Department of Panchakarma, preparation room, SDM Ayurveda Hospital, Udupi just before administering it to the animals. Matra Basti was given with Moorchita tila taila.

### Dose Fixation

The dose of the formulation was calculated by extrapolating the human dose to rat dose on basis of body surface area ratio (conversion factor 0.018 for rats) by referring to the table of "Paget and Barnes"(1969)[2] i.e.

For rats: Human dose x 0.018 = x g/ 200g rat

X x 5 – Y g/ kg/Rat

**Drugs used**

Moorchita tila taila - Matra Basti

Guduchyadi Niruha basti

Standard drug: Procyclidine.

**Chemicals used**

Various chemicals were used according to the need for the particular animal models.

To induce muscle weakness - Diazepam 4mg/body weight was used.

To induce tremors, head twitches, diarrhoea, and salivation – Oxotremorine was used.

To induce Catatonia, Sedation and Ptosis – Reserpine was used.

To check the dopamine potentiation –Dopamine was used.

**Dose Preparation**

Basti was prepared as discussed in the drug review section of this dissertation, freshly every day before the administration to the rats and was administered in dose according to the body weight of each rat. The various chemical were used in the following form, Diazepam was added with CMC (Carboxymethylcellulose sodium salt {RM10844-500G}) Procyclidine also was added with CMC (Carboxymethylcellulose sodium salt {RM10844-500G}) L-Dopa water was prepared out of L-Dopa (dihydroxyphenylalanine {RM360-5G}) and distilled water, Reserpine was added with Acetic Acid (Glacial Acetic Acid 100% GR {61784305001730}) Oxotremorine water was prepared with (Oxotremorine sesquifumarate salt {Lot#119K4613V}).

**Drug Administration**

The basti was administered using infant feeding tube No.6 through anal route and the Standard Drug was administered through the oral route. The Matra basti was administered ½ an hour after the rat was fed with food and water, whereas the Niruha basti was administered to the rat in the morning hours after maintaining overnight fasting. The standard drug was administered to the rat after being fed with food and water properly.

**Procedure**

Twenty four rats of either sex were selected and grouped into 4 groups of 6 rats each for every experimental model. The first group served as the control group. For this group the rats

were provided with normal food pellets and water ad libitum. The second group served as the Standard group where Procyclidine was administered in the specified dose orally. The third group served as the Test Drug Group, where basti was administered to the rats for 8 days. The fourth group served as the double dose group, where the basti was administered to the rats twice, maintaining same regime of the basti with a gap of ½ hour between the two basti procedures. As a poorva karma for the basti procedure, all the rats of the basti group were subjected to bahya snehana (abhyanga) with lukewarm Moorchita tila taila followed bahya swedana which was done by lukewarm Balamoola kwatha ($38^0$c) in parisheka manner, to the Abdomen and Bladder region of the rats. Guduchyadi niruha basti was given in the dose specific to rats after calculation using the Paget and Barnes Formula for dose fixation. A total of 3 Guduchyadi Niruha basti were given on the $2^{nd}$, $4^{th}$, $6^{th}$ day respectively, the niruha basti was given after keeping the rats in overnight fasting, along with a total of 5 matra basti, given on $1^{st}$, $3^{rd}$, $5^{th}$, 7th, $8^{th}$ days respectively, the matra basti was administered to the rats in full stomach. For the administration of the basti, Infant feeding tube was sieved over a 10 ml plastic syringe. The rats were held by the helper in a semi lateral position with slight inclination towards the head. The infant feeding tube was inserted into the rectum and plunger of the syringe was slowly pressed to deliver the basti solution. The temperature of the basti solution was maintained at $37^0$c to $38^0$c. Rats were provided with 200 gm of food pellets and 200ml of water. On the $8^{th}$ day, one hour after the drug administration experiments enlisted below were carried out. The following are the details of the experiments and tests conducted.

**Animal models studied**

1. Muscle tone test by Rota rod Apparatus
2. Anti-Reserpine activity
3. L-dopa potentiation test
4. Oxotremorine induced tremors test

**1. TEST FOR MUSCLE TONE AND BALANCE BY USING ROTATING ROD. (JANSSEN 1960A) (DUNHAM AND MIJA 1957)[3]**

In this method described by Janssen (1960a), the albino rats of either sex were used. Untreated rats were placed on a horizontal rotating iron rod having a diameter of 32 mm. and rotating at the rate of 24 revolutions per minute. Animals were trained for staying on the rod and walking on the rod for 2 minutes or till they fall in trial runs carried out for 3 days prior

to the actual test day. Standard and test drugs were administered by oral route and rectal route for 7 days and on the last day muscle weakening drugs (Diazepam 4mg/kg body weight) were administered and after 1 hour of drug administration these rats were placed on rod at intervals for maximum 2 minutes or until they fell down. Each animal was given three opportunities.

The effects of basti and standard drug on following parameters were noted down.

1) Time of fall (more than once)
2) Number of free rides.

**2. ANTI- RESERPINE TEST (SHETH ET AL 1972)[4]**

Basti and standard drug was administered for 7 days and on the last day, an hour after the drug administration, 2.5 mg/kg. IP reserpine was injected to the rats. They were then observed for ptosis, sedation and catatonia at every 60 minutes for 6 hours after the injection. Scores from 0-3 were given according to the intensity of the symptoms. Catatonia was measured by using wooden blocks (David et al 1979). Sedation was measured by putting the rats in the center of three concentric circles drawn on a rubber sheet. The scoring was done according to the time that the rats took to move away (vide gross behavior test). Ptosis was measured by grading the closing of eyelids. The observations were noted and are discussed further.

**3. L- DOPA POTENTIATION TEST (BARNETT.A ET. AL. 1971)[5]**

Rats of either sex were allotted to different groups as described above. Depending on the groups they were administered either basti or standard drug. L- DOPA (100 mg. /kg.) IP was injected to each rat and the behavioral changes would be noted down. If test drugs possess DOPA potentiating effect, it becomes apparent in the form of aggressive behavior. The readings were taken at 30 minutes interval, up to 6 hour after the DOPA administration. The observed behavior was assigned the subjective score in scale of 0-4 in the following manner:

1- Piloerection, slight salivation, slight increase in activity and irritability
2- Piloerection, Straub tail as event response and provoked jumping.
3- Piloerection, Straub tail and tremors.
4- Marked tremors, convulsion and death.

**4. TREMORS INDUCED BY OXYTREMORINE TEST (1977)[6]**

The basti was evaluated for anti-tremor activity by employing Oxotremorine test in rats. The procedure was similar to the one described by the plotnikojt and kastin (1977). The rats were

subjected to the basti treatment as per the described protocol. One hour after the last basti the rats were injected with Oxotremorine (500µg/ kg) through the intraperitoneal route. The resultant tremors and other symptoms were scored on an arbitrary scale of 0-3. The scoring was done at 10, 20, 40 and 60 mins after the injection of Oxotremorine. The symptoms subjected to the scoring were tremors, head twitches, ataxia, salivation, lacrimation and diarrhoea. The effect of Basti and Standard drug was observed and noted, and are discussed later.

## RESULTS

### Rota Rod Test

**Table No 2: Effect of Guduchyadi Niruha Basti on Rota Rod Apparatus.**

| **1 hour after drug administration** | | | |
|---|---|---|---|
| Groups | Initial Time Spent | Total Time Spent | Attempts |
| | MEAN ± SEM | MEAN ± SEM | MEAN ± SEM |
| Control Group | 34.12 ± 6.14 | 74.25 ± 13.15 | 3 ± 0.00 |
| Standard Group | 53.25 ± 15.18 | 93.25 ± 11.20 | 2.5 ± 0.32 |
| GNB 1 | 38.62 ± 11.19 | 76.37 ± 13.11 | 2.75 ± 0.16 |
| GNB 2 | 56.87 ± 16.28 | 97.37 ± 12.94 | 2.37 ± 0.32 |
| **After 1 hour of Diazepam injection** | | | |
| Control Group | 22.5 ± 2.93 | 71.75 ± 9.84 | 3 ± 0 |
| Standard Group | 45.87 ± 10.19 | 95.5 ± 12.33 | 2.87 ± 0.12 |
| GNB 1 | 24.25 ± 4.45 | 76.75 ± 12.79 | 3 ± 0 |
| GNB 2 | ***54.37 ± 13.16**** | 104.62 ± 13.66 | 2.5 ± 0.26 |
| **P VALUE *P<0.05** | | | |
| **After 24 hours of Diazepam injection** | | | |
| Control Group | 45.5 ± 10.61 | 88.62 ± 11.59 | 2.87 ± 0.12 |
| Standard Group | 42.87 ± 11.92 | 88.37 ± 11.95 | 2.75 ± 0.25 |
| GNB 1 | 49 ± 13.62 | 89.50 ± 11.76 | 2.75 ± 0.16 |
| GNB 2 | 52.5 ± 12.70 | 101.62 ± 11.67 | 2.62± 0.26 |

It was observed that rats of both test basti groups performed much better on the rota rod in comparison to the control group. The muscle tone of and the balance also showed significant improvement. They also committed fewer mistakes. The exact nature of this activity is not known. It may be due to increased alertness or reduced anxiety or both. This activity was seen persistent until 24 hours after diazepam injection also, thus we can conclude that this drug could is having the capacity to improve the tone of the muscles and improve balance i.e. acts as a CNS stimulant.

**Anti-reserpine test**

**Table No 3: Effect of Guduchyadi Niruha Basti on Anti Reserpine Study.**

| Groups | Ptosis | | Sedation | | Catatonia | |
|---|---|---|---|---|---|---|
| | 4TH HOUR | TOTAL | 4TH HOUR | TOTAL | 4TH HOUR | TOTAL |
| | MEAN±SEM | MEAN±SEM | MEAN±SEM | MEAN±SEM | MEAN±SEM | MEAN±SEM |
| Control Group | 2.87±0.12 | 14.37±0.70 | 2.87±0.12 | 13.62±0.98 | 2.62±0.37 | 13.87±1.64 |
| Standard Group | 2.57±0.20 | 12.37±1.06 | 2.42±0.42 | **6.42±1.54**** | 1.85±0.49 | **6.28±1.64**** |
| GNB 1 | 2.42±0.42 | **9.85±0.91**** | 2.28±0.42 | **6.71±1.56**** | **1.14±0.45*** | **4.28±1.47**** |
| GNB 2 | 2.5±0.26 | 14.25±0.81 | 2.62±0.18 | 10.25±1.01 | 1.87±0.30 | 10.37±1.37 |
| **P VALUE **P<0.01 *P<0.05** | | | | | | |

For the total values of ptosis, there was non-significant decrease, in the sedation, and catatonia parameters there was significant decrease, similarly in the GNB 1, for values of ptosis and sedation after 4 hours there was non-significant decrease but for catatonia there was significant decrease after 4 hours of reserpine injection. While considering the total values after reserpine injection there was significant decrease in all the three parameters. While considering the GNB 2 there was non-significant decrease in all the values of all the three parameters. It was found that there was considerable decrease in Cardinal symptoms of Parkinsonism i.e. sedation, catatonia (stupor), and ptosis in both the basti groups, among which GNB 1 showed highly significant results, and the GNB 2 showed moderate results. There was complete cessation of these symptoms after the 4th hour of the reserpine injection. There was improved activity and the rats also were responding to various stimuli, which can be attributed to basti drug having anti Parkinsonism activity.

**L-dopa Potentiation test**

**Table no 42: Effect of Guduchyadi Niruha Basti on L-Dopa Potentiation Test.**

| Groups | Peak Value (180 Mins) | Total |
|---|---|---|
| | MEAN ± SEM | MEAN ± SEM |
| **Control Group** | 2.5 ± 0.34 | 19 ± 2.14 |
| **Standard Group** | 3 ± 0 | 21.83 ± 1.10 |
| **GNB 1** | 2.37 ± 0.32 | 16.75 ± 1.20 |
| **GNB 2** | 3 ± 0 | 22 ± 0.21 |

In the study conducted it was seen that there was non-significant increase in the peak and the total values in both standard & GNB 2, whereas there was non-significant decrease in the values of GNB 1. This is an animal model to understand the changes in the dopamine levels that could be altered or improved by the drug studied. It was found that the basti groups

showed highly significant increase in the activities like jump, response, tremors, and Straubs tail response. There was mild increase in the GNB 1 but moderate to high increase in the GNB 2. Also there was increase in the alertness of the rats and significant increase in the activity of the rats and thus we can conclude that the Basti drug might be having a dopamine potentiating effect. I.e. it might possess highly significant anti parkinsonian activity.

**Oxotremorine test**

| **Tremors** | | |
|---|---|---|
| **Groups** | **Peak Value (40 Mins)** | **Total Value** |
| | **MEAN ±SEM** | **MEAN ±SEM** |
| Control Group | 2.5±0.22 | 10.83±0.74 |
| Standard Group | **0.66±0.33**** | **5±0.68**** |
| GNB 1 | **1.37±0.18**** | **6.5±0.65**** |
| GNB 2 | **1±0**** | **5.28±0.74 **** |
| **P VALUE **P<0.01** | | |
| **Head Twitches** | | |
| Control Group | 2±0.36 | 8.83±0.79 |
| Standard Group | **1.33±0.21** | **6.83±0.70** |
| GNB 1 | **1±0**** | **4.37±0.37**** |
| GNB 2 | **1±0**** | **5.14±0.26**** |
| **P VALUE **P<0.01** | | |
| **Ataxia** | | |
| Control Group | 2.66±0.21 | 12.83±0.60 |
| Standard Group | **0.83±0.16**** | **3.5±0.50**** |
| GNB 1 | **1.62±0.18**** | **7.87±0.47 **** |
| GNB 2 | **1±0**** | **4.14±0.55**** |
| **P VALUE **P<0.01** | | |
| **Lacrimation** | | |
| Control Group | 3±0 | 14.33±0.33 |
| Standard Group | **0 **** | **0.33±0.33**** |
| GNB 1 | **0.75±0.16**** | **3.5±0.46**** |
| GNB 2 | **1±0**** | **4.28±0.42**** |
| **P VALUE **P<0.01** | | |
| **Diarrhoea** | | |
| Control Group | 3±0 | 14.16±0.30 |
| Standard Group | **0.5±0.50**** | **6.16±0.60**** |
| GNB 1 | **0**** | **3±0.80 **** |
| GNB 2 | **1±0**** | **5.28±0.47**** |
| **P VALUE **P<0.01** | | |
| **Salivation** | | |
| Control Group | 3±0 | 14.83±0.16 |
| Standard Group | **0 **** | **4.66±0.61**** |
| GNB 1 | **1.25±0.16**** | **5.62±0.53**** |
| GNB 2 | **1±0**** | **6.14±0.14**** |
| **P VALUE **P<0.01** | | |

In the above conducted experiment various parameters, viz. Tremors, Salivation, Ataxia, Lacrimation, Head twitches, Diarrhoea, and the peak value time was noted and also total time was noted. As compared with the control group there was significant decrease in all the parameters of standard, GNB 1, and GNB 2. Proving that drug used for the study possesses the anti-parkinson activity similar to as that of the standard drug.

## CONCLUSION

In the animal experiments a total of 24 rats were subjected to each animal experimental model by dividing them in groups of 6 rats per group, groups being, control, standard, test group 1 and test group 2. From the animal experimentation done it can be concluded that, for the Rota rod apparatus test for Muscle weakness, the basti drug is having the capacity to improve the tone of the muscles and improve balance i.e. act as a CNS stimulant. In the anti-reserpine test, there was complete cessation of these symptoms after the $4^{th}$ hour of the reserpine injection. There was improved activity and the rats also were responding to various stimuli, which can be attributed to basti drug having anti Parkinsonism activity. In the L-dopa Potentiation test there was increase in the alertness of the rats, this shows significant increase in the activity of the rats and thus we can conclude that the Basti drug might be having a dopamine potentiating effect. I.e. it is having highly significant anti parkinsonian activity. Proving that drug used for the study possesses the anti-parkinson activity.

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