Effect of Saraswatarishta in animal models of behavior despair

Reshma R. Parekar, Kshitij S. Jadhav, Padmaja A. Marathe, Nirmala N. Rege

Departments of Pharmacology and Therapeutics, Seth Gordhandas Sundardas Medical College and King Edward Memorial Hospital, Parel, Mumbai, India

ABSTRACT

Background: Saraswatarishta (SA) is a herbo-mineral formulation consisting of 18 plants some of which are Medhyarasayan. It has been claimed to be useful in treating central nervous system disorders. Objective: To evaluate antidepressant effect of ‘Saraswatarishta’ (SA) alone and in combination with imipramine and fluoxetine in animal models of depression. Materials and Methods: After obtaining IAEC permission, 144 rats (n = 36/part) were randomized into 6 groups- Group 1: Distilled water (1 mL), Group 2: Imipramine (30 mg/kg), Group 3: Fluoxetine (10 mg/kg), Group 4: SA (1.8 mL/kg), Group 5: Imipramine + SA, Group 6: Fluoxetine + SA. Effects of study drugs were evaluated in forced swim test (FST) with single exposure to FST (Part 1) and repeated exposure for 14 days (Part 2). In Part 3, reserpine was used with FST and effects of study drugs were evaluated against single exposure to FST. Same model was used with repeated exposures to FST (Part 4). In each part, rats were subjected to open field test (OFT) for 5 min prior to final FST. The variables measured: Immobility time in FST; line crossing, rearing and defecation in the OFT. Results: In all four parts, individual drugs and combinations thereof produced significant decrease in immobility time as compared to control, and extent of decrease was comparable amongst these groups. However, values for combination of fluoxetine with SA group were found to be lesser than that for individual agents in Parts 2 and 3. Combination of SA with imipramine did not enhance its anti-depressant effect in any of the parts. OFT findings did not vary significantly amongst the study groups. Conclusion: Decreased immobility in FST and absence of generalized stimulation or depression of motor activity in OFT point towards potential antidepressant effect of Saraswatarishta. Its co-administration with fluoxetine showed more promising effects.

Key words: Depression, forced swimming test, reserpine, Saraswatarishta

INTRODUCTION

Depression is an affective disorder characterized primarily by change of mood. Prevalence of major depression in general population is estimated at 5% worldwide. At present 121 million people are estimated to suffer from depression. An estimated 5.8% of men and 9.5% of women experience a depressive episode in their lifetime.[1] Suicide attempts occur in approximately 15% of depressive patients, specially young and elderly men.[2]

Several different pharmacologic classes of medications are used to treat depression. Oldest agents are tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and the newer agents include selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs). Although both TCAs and MAOIs are effective, their use is limited, primarily because of adverse effects. TCAs are associated with cardiac, anticholinergic, sedative and hypotensive side effects, as well as there is potential for severe toxicity with overdose. MAOIs require adherence to dietary restrictions. Newer agents, SSRIs are also associated with side effects like somnolence, sexual dysfunction, diarrhea and weight gain.[3] Only one-third of depressed patients who are treated with a single antidepressant achieve remission (i.e., complete resolution of symptoms).[4] Although the currently prescribed drugs provide some improvement in clinical condition of patients, it is at the cost of having to bear the burden of their adverse effects. In addition, it is difficult to predict which patient

Access this article online

Quick Response Code:  Website: www.jaim.in
DOI: 10.4103/0975-9476.140469
will respond to any given treatment.\[^9\] Treatment resistant depression is a significant problem in up to two-thirds of patients with major unipolar depression.\[^9\] Hence there is a definite need for development of new antidepressants.

It was thought to be worthwhile to test indigenous drugs derived from plants in search of newer treatments of depression. In Ayurveda, formulations containing multiple herbal and herbo-mineral ingredients are often used for many different conditions based on the concept that they provide synergistic therapeutic effect and help to minimize adverse effects of major drugs.\[^8\] One such multi-ingredient plant-based herbo-mineral formulation is ‘Saraswatarishta’. It consists of 18 plants as depicted in Table 1;\[^7\] some of which include Ashwagandha, Brahmi and Shatavari which are Medhyarasayanas. Medhyarasayanas are used to improve memory and cognitive deficits.\[^7\] Saraswatarishta is claimed to be useful to treat acute anxiety, fatigue, insomnia, partial loss of memory, low grasping power, slurred speech etc.\[^8\] In view of the central nervous system effects of Saraswatarishta described in Ayurveda, it was of interest to study whether it has antidepressant potential. Hence, present study was planned to study effect of Saraswatarishta alone and its combination with the commonly prescribed antidepressants of two classes, namely imipramine and fluoxetine in animal models of behavior despair.

**MATERIALS AND METHODS**

Institutional Animal Ethics Committee permission was obtained before initiating the study. The study was conducted in accordance with the Committee for the purpose of control and supervision of experiments on animals (CPCSEA), Government of India guidelines.

**Animals**

Wistar albino rats (n = 156) of either sex weighing 180-200 g each were used. Animals used in the study were bred in the Central Animal House of the Institute (registration number 60/1999) registered with the CPCSEA. Animals were housed in polypropylene cages containing husk to keep them dry throughout the experiments. Identification of rats was done with cage number and individual marking on tail. The animals were housed under standard laboratory conditions such as room temperature at 23°C, humidity at 30-70% and with 12 h light and dark cycle. They were fed with normal rat chow procured from Nav Maharashtra Chakan Oil Mills Ltd, Maharashtra and Aquaguard pure water in polyethylene bottle given ad libitum.

**Drugs**

*Saraswatarishta* (SA) was purchased (Sandu Brothers Pvt. Ltd.) and was stored at room temperature throughout the experiment. SA was administered orally in the dose of 1.8 mL/kg/day. Ingredients of SA are *Bacopa Moniera, Asparagus racemosus, Pueraria tuberosa, Terminalia chebula, Zinziber officinalis, Anethum sowa, Operculina ipomoea, Piper longum, Syzygium aromaticum* Merr. perry. *Acorus calamus,* *Saussurea lappa,* *Withania somnifera,* *Terminalia bellerica,* *Tinospora cordifolia*, *Elettaria cardmonnum, Embelia ribes, Cinamomum zelonica* and pure gold.\[^8\] Imipramine (Torrent Pharma Ltd., Ahmadabad) and fluoxetine (Sun Pharma Ltd.) were dissolved in distilled water and administered orally. Reserpine (Sun Pharma Ltd.) was administered subcutaneously. Distilled water (in equal volume) was administered orally to the vehicle control group.

**Study Procedure:** Study was conducted in four different parts as shown in Figure 1.

Part 1: In this part, standardization of animal model of behavioral despair was carried out.

Rats were subjected to forced swimming test (FST) along with reserpine pretreatment.\[^8\] Animals were forced to swim for 15 min on Day 1. On Day 2, distilled water and reserpine (2.5 mg/kg) were injected subcutaneously to

### Table 1: Ingredients of Saraswatarishta

| Name of the plant          | Common name         | Part of plant |
|----------------------------|---------------------|--------------|
| Bacopa Moniera Linn.       | Brahma              | Fruit        |
| Asparagus racemosus Wild.  | Shatavari           | Root         |
| Pueraria tuberoso          | Vidarikand          | Tuber        |
| Terminalia chebula Retz.   | Hirda               | Fruit        |
| Zinziber officinalis Roscoe.| Ardrak             | Tuber        |
| Anethum sowa Roxb.         | Sounfi/Mishreya     | Seed powder  |
| Operculina ipomoea Linn.   | Harenuka/Trivrut    | Seed         |
| Piper longum Linn.         | Pippali             | Fruit        |
| Syzygium aromaticum Merr  | Lavang              | Flower       |
| Acorus calamus Linn.       | Vekhand             | Root         |
| Saussurea lappa            | Kusthham            | Toot         |
| Withania somnifera Dunal.  | Ashwagandha         | Root         |
| Terminalia bellerica Roxb. | Behada              | Fruit        |
| Tinospora cordifolia Wild  | Guduchi             | Tuber        |
| Elettaria cardmonnum Maton.| Velachi             | Fruit/seed   |
| Embelia ribes Burm. F.     | Vidang              | Fruit/seed   |
| Cinamomum zelonica Blume.  | Dalchini            | Bark         |
| Mineral                    | Suvarana            | Intact       |
the two groups of rats. Half an hour later, the rats were subjected to forced swimming session for 6 min.

Part 2A: This part was planned to explore effects of \( \text{SA} \), concomitant administration of \( \text{SA} \) with imipramine and \( \text{SA} \) with fluoxetine in the model of behavioral despair induced by forced swimming in rats. This part was further subdivided to study effect on single exposure to FST (Part 2A-I) and on repeated exposure for 14 days (Part 2A-II). Rats (n = 36/subpart) were randomized into 6 treatment groups as follows: Group 1: Distilled water (1 mL), Group 2: Imipramine (30 mg/kg), Group 3: Fluoxetine (10 mg/kg), Group 4: \( \text{SA} \) (1.8 mL/kg), Group 5: Imipramine + \( \text{SA} \), Group 6: Fluoxetine + \( \text{SA} \).

In Part 2A-I, first FST was conducted on Day 1 for 15 min. The animals were then administered the respective drugs: 24, 5 and 1 hour/s prior to next forced swimming test. On Day 2, the rats were subjected to OFT for 5 min and then to FST for 6 min.

For Part 2A-II, study drugs were administered for 14 days to the respective groups with daily forced swimming sessions for 6 min. On Day 15, they were subjected to open field test (OFT) and then the final FST was conducted for 6 min.

Part 2B: Reserpine was used along with FST and the effects of \( \text{SA} \), concomitant administration of \( \text{SA} \) with imipramine and \( \text{SA} \) with fluoxetine were evaluated. This part also was subdivided to study effects against single exposure to FST and reserpine (Part 2B-I) and on repeated exposure to FST for 14 days followed by reserpine (Part 2B-II). Rats (n = 36 per subpart) were randomized into 6 treatment groups as follows: Group 1: Distilled water (1 mL), Group 2: Imipramine (30 mg/kg), Group 3: Fluoxetine (10 mg/kg), Group 4: \( \text{SA} \) (1.8 mL/kg), Group 5: Imipramine + \( \text{SA} \), Group 6: Fluoxetine + \( \text{SA} \).

In Part 2B-I, first FST was conducted on Day 1 for 15 min. The animals were then administered the respective drugs: 24, 5 and 1 hour/s prior to next forced swimming test. On Day 2, reserpine (2.5 mg/kg) was injected subcutaneously. Thirty minutes later, the rats were subjected to OFT for 5 min and then to FST for 6 min.

For Part 2B-II, the study drugs were administered for 14 days to the respective groups with daily forced swimming sessions for 6 min. On Day 15, reserpine (2.5 mg/kg sc) was injected. Thirty minutes later, the rats were subjected to OFT for 5 min and then to FST for 6 min.

The variable measured was immobility time in FST and frequency of activities by animals (line crossing, rearing and defecation) in the OFT. For all experiments, the observer was blinded to the treatment groups.

**Statistical analysis**

The data was expressed in the form of mean ± SD.
Immobility time in FST and frequencies of line crossing, rearing and defecation in OFT were compared using ANOVA with post hoc Dunnet’s test. The level of significance was set at $P < 0.05$. The GraphPad InStat software version 3.06 was used for statistical analysis.

RESULTS

Part 1: Standardization of experimental models of behavioral despair and depression

In this standardization phase, the rats given distilled water exhibited immobility time of $179.19 \pm 8.47$ s. In reserpine-treated rats, a significant rise in immobility time ($256.03 \pm 28.11$ s) was observed compared to distilled water treated rats ($P < 0.001$).

Part 2A-I: Model of FST

As depicted in Figure 2, the rats in the distilled water control group exhibited immobility time of $175.39 \pm 3.95$ s. The groups of rats pretreated with imipramine, fluoxetine, $S.A$, combination of $S.A$ with imipramine and combination of $S.A$ with fluoxetine showed significantly less immobility time as compared to the distilled water control group and the shortest immobility time was noted in group receiving imipramine ($78.88 \pm 21.19$ s). Addition of $S.A$ to either imipramine or fluoxetine did not result in further statistically significant reduction of immobility time compared to imipramine and fluoxetine alone. Further, the reduction in immobility time observed in rats treated with imipramine, fluoxetine, $S.A$ and the combination was comparable among each other.

There was statistically significant decrease in the locomotor activity in all the study drug groups compared to the vehicle control group except for fluoxetine, which showed more pronounced decrease in locomotor activity ($P < 0.05$) compared to control group.

Part 2A-II: Chronic version of FST

Immobility time exhibited by rats in the distilled water control group was found to be $168.80 \pm 12.71$ s [Figure 3]. The rats treated with imipramine, fluoxetine, Saraswatarishta ($S.A$) as well as combination (imipramine with $S.A$ and fluoxetine with $S.A$) for 14 days and exposed to FST repeatedly exhibited significantly low values of immobility time compared to distilled water control group. The groups of rats which received imipramine, fluoxetine and $S.A$ alone and the combination groups showed comparable immobility time. The combination groups did not show any further reduction in immobility time as the values were found to be comparable to either drug given alone. However, co-administration of fluoxetine with $S.A$, showed a trend towards further reduction in immobility time ($79.84 \pm 6.78$ s) than either drug alone. As depicted in Table 3 the frequencies of locomotion, rearing and defecation did not vary significantly from the control group values in all the study drug groups except for fluoxetine, which showed more pronounced decrease in locomotor activity ($P < 0.05$) compared to control group.

Part 2B-I: FST in reserpine pretreated rats

The control group in this experiment showed more prolonged immobility time ($250.03 \pm 16.25$ s) compared to the control group subjected to forced swimming alone in part 2A-I ($175.39 \pm 3.95$ s). Immobility time was found to decrease significantly in rats treated with imipramine, fluoxetine, $S.A$ and combination of imipramine and $S.A$ or fluoxetine and $S.A$ [Figure 4]. The immobility time of fluoxetine group was higher than that of imipramine group; the values of immobility time in imipramine, fluoxetine, $S.A$ groups were comparable statistically. Concomitant administration of imipramine and $S.A$ did not cause further reduction in immobility time and the immobility time of this group remained comparable to that of imipramine. Concomitant administration of fluoxetine and $S.A$ however caused some more reduction in immobility time as compared to fluoxetine alone. The extent of reduction

![Figure 2: Immobility time in acute FST](image1)

![Figure 3: Immobility time in chronic version of FST](image2)
in the fluoxetine with SA group was comparable to that of fluoxetine or SA alone.

As depicted in Table 4, reserpine pre-treatment definitely reduced the locomotor activity and frequency of rearing in the control group animals when compared to animals subjected to FST alone in parts 2A-I [Table 2] and 2A-II [Table 3]. Locomotion and frequency of rearing appeared to have increased in animals treated with the study drugs and the increase was statistically significant in SA and imipramine with SA groups when compared to control. In imipramine, SA and the two combination groups, the rearing frequencies were found to increase significantly as compared to the vehicle control group. Rise in both locomotion as well as rearing was comparable among one another for SA, imipramine with SA, fluoxetine and fluoxetine with SA groups. Defecation rate remained comparable across all the study drug groups.

**Part 2B-II: Chronic version of FST in reserpine pretreated rats**

Immobility time exhibited by rats of the control group given reserpine after repeated exposures to FST was found to be 248.86 ± 12.69 s [Figure 5]. This time was prolonged compared to rats given only a single exposure to FST and no reserpine (as in Part 2A-II: 168.80 ± 12.71 s). A significant reduction in immobility time was found in the groups treated with imipramine, fluoxetine, SA, and the two combination groups. In contrast to the acute model, wherein the immobility time of fluoxetine group was higher (152.43 ± 19.30 s) than that of imipramine group, this experiment showed that on chronic administration of fluoxetine, the immobility time reduces further (107.77 ± 18.70 s) and was found to be comparable to both, imipramine and Saraswatarishta given alone. Concomitant administration of imipramine and Saraswatarishta or fluoxetine and Saraswatarishta did not cause further reduction in immobility time as the immobility times of these groups were comparable to that of imipramine or Saraswatarishta alone.

As observed in Part 2B-I, in this part too, reserpine pre-treatment reduced locomotor activity and frequency of rearing in control group animals. As shown in Table 5 all the study drug groups showed increased locomotor activity but statistically significant improvement was seen in fluoxetine, SA, fluoxetine with SA groups. Effect on

---

**Table 2: Part 2A-I - Open field test in model of FST**

| Group no | Groups (n=6/group) | Locomotion (Number per 5 min) | Rearing (Number per 5 min) | Defecation (Number per 5 min) |
|----------|--------------------|-------------------------------|-----------------------------|-----------------------------|
| 1        | Distilled water (5 mL/kg) | 55.67±6.28                   | 26.67±2.6                  | 2.67±1.7                   |
| 2        | Imipramine (30 mg/kg)    | 28.67±18.82**                | 18.67±2.6                  | 3.00±1.79                   |
| 3        | Fluoxetine (30 mg/kg)    | 33.67±6.74                  | 21.67±2.6                  | 4.67±2.14                   |
| 4        | Saraswatarishta-SA (1.8 mL/kg) | 36.67±10.03*               | 30.67±2.6                  | 2.33±2.25                   |
| 5        | Imipramine+SA            | 29.00±11.73**               | 24.00±1.6                 | 4.67±2.14                   |
| 6        | Fluoxetine+SA            | 27.33±13.85                 | 20.67±2.6                 | 3.83±1.6                   |

Figures represent mean±SD using ANOVA with post hoc Dunnet’s test. **P<0.05, NS: Non significant vs Distilled water control, NS1: Not significant vs Imipramine, NS2: Significant vs Fluoxetine, FST=Forced swim test, OFT=Open field test.

**Table 3: Part 2A-II - Open field test in model of chronic FST**

| Group no | Groups (n=6/group) | Locomotion (Number per 5 min) | Rearing (Number per 5 min) | Defecation (Number per 5 min) |
|----------|--------------------|-------------------------------|-----------------------------|-----------------------------|
| 1        | Distilled water (5 mL/kg) | 44.67±6.28                   | 24.67±2.6                  | 2.83±2.04                   |
| 2        | Imipramine (30 mg/kg)    | 31.50±9.79                   | 22.67±2.6                  | 4.67±1.79                   |
| 3        | Fluoxetine (30 mg/kg)    | 23.67±7.66                  | 13.67±2.6                  | 3.50±2.09                   |
| 4        | Saraswatarishta-SA (1.8 mL/kg) | 29.67±14.33**              | 21.67±2.6                  | 3.33±1.6                   |
| 5        | Imipramine+SA            | 33.33±13.05**               | 23.67±2.6                  | 3.83±1.6                   |
| 6        | Fluoxetine+SA            | 34.33±14.32                 | 20.67±2.6                 | 3.75±3.0                   |

Figures represent mean±SD using ANOVA with post hoc Dunnet’s test. **P<0.05, NS: Non significant vs Distilled water control, NS1: Not significant vs Imipramine, NS2: Not significant vs Fluoxetine, OFT=Open field test, FST=Forced swim test.
reserpine has been administered intraperitoneally and subcutaneously to induce depression in animals.\[12,13\] The range of reserpine dose is wide between 0.5 and 6.0 mg/kg but higher doses up to 8 mg/kg have also been used.\[12,13\] In our study, we chose to use reserpine along with FST to simulate the behavioral and neurochemical mechanisms involved in clinical depression and it was decided to test Saraswatarishta in two different models in acute and chronic settings. We selected a dose of 2.5 mg/kg of reserpine and administered subcutaneously. This dose was found to increase the immobility time in FST significantly.

As seen from the results, both the time tested antidepressants exerted positive effects in the present study. However, effects produced by imipramine were found to be better when compared to other two drugs viz. fluoxetine and Saraswatarishta. This may be attributable to the additional anticholinergic and antihistaminic activity of imipramine since anticholinergics and antihistaminics also show positive results in FST model.\[13\] Saraswatarishta was found to decrease the immobility time in both the models of behavioral despair. Reserpine pretreated rats when subjected to FST showed further prolongation of immobility time than those subjected to FST alone. Improvement in the state of immobility by Saraswatarishta on both short and long term administration; analogous to modern antidepressants indicates its antidepressant potential. Saraswatarishta although is used as Medhyarasayana, in Ayurveda clinical practice since many years, no studies have been done to evaluate its antidepressant activity until recently. A study by Gupta et al., showed the antidepressant activity of Saraswata choorna as compared to imipramine in the forced swimming test paradigm.\[14\] Our study substantiate the findings of

**DISCUSSION**

In the model of behavioral despair, which was used in the present study, single and repeated exposures to FST were given. This was to simulate the clinical scenario, wherein stressful stimulus may be acute or may be a chronic one. Reserpine has been used in the past to induce depression for evaluating antidepressants.\[10,11\] Reserpine depletes central and peripheral monoamines with decreased locomotor activity in rodents. The reserpine effect reversal test, designed by Costa et al., was the first attempt to screen imipramine-like drugs to demonstrate its antidepressant effect.\[11\] Reserpine

---

**Table 4: Part 2B-I - Open field test in model of FST (with reserpine pre-treatment)**

| Group No. | Groups (n=6/group) | Locomotion (Number per 5 min) | Rearing (Number per 5 min) | Defecation (Number per 5 min) |
|-----------|--------------------|-------------------------------|---------------------------|-------------------------------|
| 1         | Distilled water (Reserpine control) | 9.00 ± 3.41                  | 4.17 ± 2.56               | 2.00 ± 1.90                   |
| 2         | Imipramine (30 mg/kg) | 28.33 ± 18.29*               | 20.00 ± 5.80***           | 2.00 ± 2.28 NS               |
| 3         | Fluoxetine (10 mg/kg) | 32.33 ± 21.08*               | 14.17 ± 8.80*            | 2.17 ± 1.33                   |
| 4         | Saraswatarishta (1.8 mL/kg) | 35.67 ± 11.27*               | 23.83 ± 4.71              | 3.17 ± 1.33                   |
| 5         | Imipramine + SA        | 39.17 ± 15.33***             | 24.17 ± 11.41***          | 4.17 ± 3.31                   |
| 6         | Fluoxetine + SA        | 30.83 ± 10.34*               | 17.83 ± 6.94              | 1.50 ± 1.38                   |

Figures represent mean ± SD using ANOVA with post hoc Dunnet’s test.:*p < 0.05, ***p < 0.01

**Table 5: Part 2B-II - Open field test in model of chronic FST (with reserpine Pre-Treatment)**

| Group No. | Groups (n=6/group) | Locomotion (Number per 5 min) | Rearing (Number per 5 min) | Defecation (Number per 5 min) |
|-----------|--------------------|-------------------------------|---------------------------|-------------------------------|
| 1         | Distilled water (Reserpine control) | 7.67±7.58                    | 7.50±12.05                | 2.50±1.64                     |
| 2         | Imipramine (30 mg/kg) | 25.83±13.19 NS               | 17.00±3.52 NS            | 4.50±2.43 NS                   |
| 3         | Fluoxetine (10 mg/kg) | 37.33±13.63*                 | 23.67±5.72 NS            | 6.00±3.95 NS                   |
| 4         | Saraswatarishta (1.8 mL/kg) | 26.50±12.16*                | 16.17±8.04 NS            | 3.67±3.14 NS                   |
| 5         | Imipramine+SA        | 23.17±9.24 NS                | 20.50±5.54 NS            | 4.83±2.71 NS                   |
| 6         | Fluoxetine+SA        | 20.00±17.09*                | 14.17±4.02 NS            | 2.50±3.33 NS                   |

Figures represent mean ± SD using ANOVA with post hoc Dunnet’s test.:*p<0.05, ***p<0.001, NS: Non significant vs Distilled water control

---

**Figure 5: Immobility time in chronic version of FST with reserpine**

Rearing was reversed by all the treatment groups. Rearing frequencies increased significantly in fluoxetine and imipramine with SA groups. Defecation rate was similar across all the study drug groups.
Gupta et al., and provides further evidence of antidepressant like effects of Saraswatarishta.

The specificity of FST for antidepressant evaluation has been questioned as a large number of non-antidepressants also reduce immobility. False positive results have been reported for stimulants, anticholinergics, antihistaminics, pentobarbital and opiates. Hence, to rule out non-specific stimulant or depressant effect, an open field test (OFT) was conducted. There was comparable decrease in locomotor activity in Saraswatarishta, imipramine, fluoxetine and the two combination groups in acute and chronic FST tests when compared to control group. Reserpine pretreatment dampened locomotion and rearing, which was reversed by all the study drugs. Again the rise in locomotion and in rearing among the study drug groups were found to be comparable. The responses to OFT were consistent in chronic FST in reserpine pretreated animals in Part 2B-II. The changes produced in OFT by Saraswatarishta were similar to the modern medicines in all four experiments. The findings of no overt motor dysfunction due to Saraswatarishta in OFTs confirm possibility of its antidepressant like effect and rule out its nonspecific stimulant or depressant effect.

The concurrent administration of imipramine with Saraswatarishta failed to exert better effect than either drugs alone in acute and chronic version of FST. There was a small trend towards better effect with combination of fluoxetine with Saraswatarishta than the individual drug groups chronic version of FST, and in acute FST in reserpine pretreated rats, fluoxetine with Saraswatarishta group showed a trend towards better effect as compared to fluoxetine alone. It is unclear why the effect of this combination was not consistent throughout all experiments of the study and also why the combination of Saraswatarishta with imipramine did not show such a trend. It can be speculated that imipramine and Saraswatarishta share same mechanism of action and hence there was no enhanced effect, whereas fluoxetine and Saraswatarishta complement effects of one another in some way.

At this stage it is not possible to speculate mechanism/s by which ‘Saraswatarishta’ exerts its effects. FST serves as a stressor and induces alterations in the hypothalamic-pituitary-adrenal-axis to increase corticosterone levels in blood. Various types of stressors that induce hormonal alterations in experimental animals also produced similar effects in human as observed in depressed patients. Perhaps estimation of monoamine levels in the brain (neurochemical mechanism) and monoamine oxidase activity (biochemical mechanism) and studies with mediators of HPA axis would help in unraveling the mechanism by which ‘Saraswatarishta’ acts and then its effects can be better interpreted.

**CONCLUSIONS**

Thus, present study proved that Saraswatarishta exerts antidepressant effects on its own. Concomitant administration with imipramine did not enhance its anti-depressant effect. Effect of co-administration of Saraswatarishta with fluoxetine appears promising but needs to be evaluated further to study their precise interaction.

**REFERENCES**

1. Shalam Md, Shantkumar SM, Narasu LM. Pharmacological and biochemical evidence for the antidepressant effect of the herbal preparation Trans-01. Indian J Pharmacol 2007;39:231-4.
2. Modabernia MJ, Tehrani HS, Fallahi M, Shirazi M, Modabbernia AH. Prevalence of depressive disorders in Rasht, Iran: A community based study. Clin Pract Epidemiol Ment Health 2008;4:20.
3. O’Donnell JM, Shelton RC. Drug therapy of depression and anxiety disorders. In: Brunton LL, Chabner BA, Knollmann BC, editors. Goodman and Gilman’s The pharmacological basis of therapeutics. 12th ed. New York: McGraw Hill; 2011. p. 400-3.
4. Adams SM, Miller KE, Zylstra RG. Pharmacologic Management of Adult Depression. Am Fam Physician 2008;77:785-92.
5. Little A. Treatment-Resistant Depression. Am Fam Physician 2009;80:167-72.
6. Bhattacharya SK. Behavioural Studies on BR-16A (Mentat), A Herbal Psychotropic Formulation. Indian J Exp Biol 1994;32:37-49.
7. Atha Vajikaranaprakaranam. In: Shastri RV, editor. Bhaisajyaratnavali, Vidyotini – Hindiyakhya – Vimarsh-Parishishtasahita. Varanasi: Chaukhamba Sanskrit Bhavan; 2002. p. 796-7.
8. Atha Rasayanaprakaranam. In: Shastri RV, editor. Bhaisajyaratnavali, Vidyotini – Hindiyakhya – Vimarsh-Parishishtasahita. Varanasi: Chaukhamba Sanskrit Bhavan; 2002. p. 775-6.
9. Huang QJ, Jiang H, Hao XL, Minor TR. Brain IL-1 like effects of imipramine, desipramine and dosulepin in the forced swimming test in rats. Acta Pharmacol Sin 2004;25:293-6.
10. Bernardi D, Pagliuca S, Jori A. Peripherical and central, component in the hypothermic, effect of desipramine in reserpinised rats. J Pharm Pharmacol 1968;20:204-9.
11. Cotter-Deubiere B, Chenu F, Bourbon M. Forced swimming test in mice: A review of antidepressant activity. Psychopharmacology (Berl) 2005;177:245–55.
12. Kuczynski R. Differential effects of reserpine and tetrodazabenzalzine on rat striatal synaptosomal dopamine biosynthesis and synaptosomal dopamine pools. J Pharmacol Exp Ther 1977;201:357-67.
13. Vogel GH, editor. Drug Discovery and Evaluation of Pharmacological Assay. New York: Springer-Verlag and Berlin: Heidelberg; 2002.
14. Kaur G, Kulkarni SK. Selective Alpha,-Adrenoceptor Blockade Produces Antidepressant Effect in Mice. Indian J Pharmacol 1998;30:394-8.
15. Butterweck V, Nishibe S, Sasaki T, Uchida M. Antidepressant effect of apocynum venetum leaves in a forced swimming test. Biol Pharma Bull 2001;24:848-51.
16. Gupta K, Ashok BK, Ravishankar B, Thakar AB. Anti-anxiety and anti-depressant activities of Sarasvata choorna in experimental animals. Ayu 2011;32:590-3.

How to cite this article: Parekar RR, Jadhav KS, Marathe PA, Rege NN. Effect of Saraswatarishta in animal models of behavior despair. J Ayurveda Integr Med 2014;5:141-7.

Source of Support: Nil, Conflict of Interest: None declared.