Research Article

www.ijrap.net

(ISSN Online:2229–3566, ISSN Print:2277–4343)

CNS DEPRESSANT ACTIVITY OF KASHAYA OF ASOKA – *SARACA ASOCA* ROXB. DE (WILDE.)

Asha S Raj [1]*, Sara Monsy Oommen [2]

[1] Domain expert, Department of Dravyaguna, Institute of Teaching and Research in Ayurveda, Jamnagar, India

[2] Professor and HOD, Department of Dravyaguna, Government Ayurveda College, Kannur, India

Received on: 10/11/23 Accepted on: 02/01/24

***Corresponding author**

E-mail: drashasomaraj@gmail.com

DOI: 10.7897/2277-4343.15113

ABSTRACT

Ayurveda explains chikitsa (treatment – mode to attain health) as a conglomeration of chatushpada's (four limbs). Pharmacological categorization of drugs can be explored for the first time from the Charaka Samhita, Shadvirechana Shatasriteeya Adhyaya. Asoka - *Saraca asoca* [Roxb] de Wilde has been included in the Vedanasthapana mahakashaya (group of drugs which alleviates a specific sensation) mentioned by Acharya Charaka, which is explained as streenam uchrokanashanaya by the Nighantukaara's. The etymology of soka is chittavikalatha, which is a 'lead' to the action of a drug on "manasika bhava's". In clinical experience, apart from the pain, associated symptoms like nausea, vomiting, delirium, insomnia, emotional instability, nervousness, irritability, anger, and fear are also relieved by its usage. Till now, the pharmacological action of Asoka on "manasika bhava's" remains unexplored. Hence, a preliminary experimental study has been undertaken on the reverse pharmacological aspect to assess the action of this drug on CNS. The depressant action of drugs on CNS is mediated through both neural and hormonal mechanisms. The immediate reduction in spontaneous motor activity was achieved through the neural mechanism, and the prolonged effect was achieved through the hormonal action. The drug possesses bitter principles. The functional bitter taste is expressed in brain cells by bitter taste receptors T2R's. T2R-4, T2R-107, and T2R-38 transcripts are found in the brain stem, cerebral cortex and cerebellum. The drug is a potent source of phytoestrogen, which has oestrogen-mimicking action. The drug significantly reduces spontaneous motor activity in the CNS depressant activity study on all assessment days, with a p-value<0.001.

Keywords: CNS depressant activity, Reverse Pharmacology, *Saraca asoca*, Stem bark, *Kashaya*

INTRODUCTION

Ayurveda is the indigenous system of medicine in India. The word itself means "knowledge for longevity". It explains chikitsa (treatment – mode to attain health) as a conglomeration of chatushpada's (four limbs). After Vaidya (physician), dravya (drug) has been considered as the prime object responsible for successful treatment. Pharmacological categorization of drugs can be explored for the first time from the Charaka Samhita, Shadvirechana Shatasriteeya Adhyaya. In the chapter, about 50 groups of drugs with specific indications are grouped as Mahakashaya and explained in detail.[1]

Asoka - *Saraca asoca* [Roxb] de Wilde has been included in the Vedanasthapana mahakashaya (group of drugs that alleviate a specific sensation) mentioned by Acharya Charaka. Acharya Chakrapani explains that Vedanasthapana dravya alleviate vedana (pain or uneasiness) and results in prakrutisthapana (removal of uneasiness and restoration of health). Asoka has been used as arista (alcoholic preparation) in clinical conditions like dysmenorrhea as a spasmodic pain reliever.

Nighantukara's interpret Asoka as "streenam ucchokanasanaha", sokanashana.[2] The etymology of soka is chittavikalatha, which is a 'lead' to the drug's action on "manasika bhava's". In clinical experience, apart from the pain, associated symptoms like nausea, vomiting, delirium, insomnia, emotional instability, nervousness, irritability, anger, and fear are also relieved by its usage.[3] Till now, the pharmacological action of Asoka on "manasika bhava's" remains unexplored. Hence, a preliminary experimental study has been undertaken in the reverse pharmacological aspect to assess the drug's action on the Central Nervous System.

This study approaches the Vedanasthapana property of the drug in a reverse pharmacological aspect. Apart from the clinical evidence, the CNS depressant activity of the study has not yet been validated. Prevalent CNS depressants are highly dose-dependent and cause cognitive impairment, memory loss and withdrawal symptoms on prolonged use. If an effective herbal remedy can replace these drugs, it will be a boon to society.

MATERIALS AND METHODS

The study was conducted on Male and female Swiss albino mice weighing 20 to 30 g using Kashaya (traditional aqueous extract) of stem bark of Asoka - *Saraca asoca* (Roxb.) de Wilde., feeding cannula, gloves, weighing balance, feeding bottle, syringes, Actophotometer, cotton, 70% alcohol. The study was conducted after getting approval from IAEC with registration number GAVC/IAEC/2016-1/P_3.

CNS depressant activity was assessed by evaluating spontaneous motor activity using an Actophotometer using Swiss albino mice of both sexes. The study was conducted in four groups of 6 animals each. The control group was treated with normal saline, and the test groups were treated respectively with half effective dose, effective dose, and double effective dose of kashaya of stem bark of Asoka – *Saraca asoca* (Roxb.) de Wilde. The spontaneous motor activity was assessed by placing the animal for 6 min inside the chamber of the Actophotometer, and the number of beam breaks was counted. This was done before administration of the test drug and after 30 min, 60 min, 90 min and 120 min of drug administration. The medicine was given continuously for 14 days, and assessments were done on the 0^{th}, 7^{th} and 14^{th} day.

Preparation of test drug

The stem bark of Asoka-*Saraca asoca* (Roxb.) de Wilde was collected from an authentic source, washed with water to remove impurities and dried. The dried stem bark was crushed coarsely. The test drug was prepared by boiling 1 pala (48 g) of coarsely crushed stem bark of Saraca asoca (Roxb.) de Wilde. in 16 parts (768 litres) of water over the mild fire and reduced to 1/8 part (96 litres) of the original quantity.[4] The test drug was filtered to ensure free flow throughout the oral gavage.

Dose of test drug

Human dose for kashaya is 48ml as per AFI. The dose of the drugs was calculated by extrapolating the therapeutic dose to the effective mice dose by using the conversion factor given by Paget and Barnes Table (1964), which is based on the body surface area ratio. The conversion factor for the mouse dose corresponding to the human dose is 0.0026.

Animal dose = Human dose × 0.0026 for 20 g mouse
= 48ml × 0.0026 = 0.1248 ml/20 g mouse
= 0.1248 ml/20 g of mouse

For the CNS depressant study, the drug is given in the following doses: 1/2X, X, and 2X, where 'X' represents the calculated effective dose of the test drug.

Design of animal experiment

The study was conducted on 24 Swiss albino mice, 12 male and 12 female, with about 20-30 g body weight. The drug was given continuously for 14 days. CNS depressant activity was assessed using an Actophotometer on the 0th, 7th and 14th day. It is recorded as basal just before the drug administration and 30, 60, 90 and 120 min after drug administration.[5]

Figure 1: Lateral view of Actophotometer

Figure 2: Aerial view of Actophotometer

Table 1: Grouping of animals for CNS depressant activity

Groups	Treated with	The dose of the drug administered
Group A	Normal saline	0.2 ml per 20 g b.wt
Test group 1	Kashaya of stem bark of *Saraca asoca* (Roxb) de Wilde [1/2X]	0.0624 ml per 20 g b.wt
Test group 2	Kashaya of stem bark of *Saraca asoca* (Roxb) de Wilde [X]	0.1248 ml per 20 g b.wt
Test group 3	Kashaya of stem bark of *Saraca asoca* (Roxb) de Wilde [2X]	0.2496 ml per 20 g b.wt

Grouping of animals

The animals were divided into 4 groups of 6 mice each: 3 male and 3 female. Group A served as control and received normal saline at a dose of 0.2ml per 20g b.wt of mice. TG1, TG2 & TG3 are test groups that received the calculated effective dose, half the calculated effective dose, and double the estimated effective dose.

Procedure

Animals within the weight range were grouped, and the dose was calculated using Paget and Barn's table. Drugs were given using oral gavage as a single dose for 14 days. CNS depressant activity was assessed by evaluating the spontaneous motor activity of mice by placing them inside an Actophotometer for 6 min. Actophotometer consists of a square chamber equipped with photoelectric cells producing light beams. Motor activity was assessed by counting the number of beam breaks occurring for 6 min. The activity was assessed before drug administration and 30, 60, 90, and 120 min after drug administration on 1st day. Further assessment was done on the 7th & 14th day. The Actophotometer was cleaned with a cotton swab dipped in 70% alcohol between the observations.

Table 1: Effect of kashaya of stem bark of Asoka – *Saraca asoca* (Roxb.) de Wilde on both sexes of mice in reduction of spontaneous motor activity with time – On Day 0

Group/Sex	F(w)-value	F(w) – value	F(b) - value
Control			
Female	1.654^{NS}	1.695^{NS}	0.109^{NS}
Male	0.423^{NS}		
TG1 – 1/2X			
Female	0.457^{NS}	2.889^{NS}	0.957^{NS}
Male	9.336**		
TG2 – X			
Female	0.927^{NS}	1.159^{NS}	0.662^{NS}
Male	0.889^{NS}		
TG3 – 2X			
Female	13.96***	11.21***	0.080^{NS}
Male	3.622^{NS}		

Table 2: Effect of kashaya of stem bark of Asoka – *Saraca asoca* (Roxb.) de Wilde on both sexes of mice in reduction of spontaneous motor activity with time - Day 7

Group/Sex	F(w) – value	F(w) – value	F(b) - value
Group A			
Female	1.608^{NS}	0.868^{NS}	1.020^{NS}
Male	0.662^{NS}		
TG1 – 1/2X			
Female	11.13**	3.818^{*}	1.501^{NS}
Male	0.591^{NS}		
TG2 – X			
Female	38.26***	12.26^{***}	4.043*
Male	2.916^{NS}		
TG3 – 2X			
Female	7.122**	6.395**	2.288^{NS}
Male	2.491^{NS}		

Table 3: Effect of kashaya of stem bark of Asoka – *Saraca asoca* (Roxb.) de Wilde on both sexes of mice in reduction of spontaneous motor activity with time- Day 14

Group/Sex	F(w) - value	F(w) – value	F(b) – value
Group A			
Female	0.589^{NS}	0.349^{NS}	0.888^{NS}
Male	1.513^{NS}		
TG1 – 1/2X			
Female	7.942**	6.003**	0.676^{NS}
Male	1.494^{NS}		
TG2 – X			
Female	6.303*	11.47***	2.137^{NS}
Male	12.63**		
TG3 – 2X			
Female	20.03***	25.90***	6.883^{NS}
Male	6.742*		

RESULTS

On the 0^{th} day, reduction in spontaneous motor activity within time in both sexes of mice had no significance in Group A(Control) and TG2(X). In TG1(1/2X), the reduction of spontaneous motor activity in males is remarkably lower at 120 min than in females. It gives an F-value within the male group as 9.336, with a p-value significant of less than 0.01. In TG3, the reduction of spontaneous motor activity in females achieved its maximum at +90 min. It gives an F-value of 13.96, with a p-value significant at less than 0.001.

On the 0^{th} day, reduction in spontaneous motor activity within and between groups has no significance for Group A, TG1(1/2X) and TG2(X). In TG3(2X), spontaneous motor activity reduces gradually, and the maximum reduction was attained at 90 min. For TG3(2X), the F-value calculated within the group is 11.21, which gives a p-value (0.000) less than the significance level of 0.001. The reduction of spontaneous motor activity has no statistical significance between the groups. (Table 1)

On the 7^{th} day, reduction in spontaneous motor activity within time in both sexes of mice had no significance in Group A(Control).

In TG1(1/2X), the reduction of spontaneous motor activity was gradual in both sexes of mice and attained maximum reduction at 90 min and, after that, slightly decreased at 120 min. It gives an F-value within the female group as 11.13, with a p-value (0.023) significant at a level less than 0.01, whereas in males, the reduction has no statistical significance.

In TG2(X), females got a gradual reduction of spontaneous motor activity, whereas males followed an irregular curve. The females attain a maximum decrease at 120 min, with an F-value of 38.26, which gives a p-value (0.000) significant at a level less than 0.001.

In TG3, the reduction of spontaneous motor activity in females forms a steep straight line and achieves its maximum at 120 min.

It gives an F-value of 7.122, which provides a p-value with (0.003) significant at a level less than 0.001.

On the 7th day, the reduction in spontaneous motor activity within and between groups has no significance for Group A. In TG1(1/2X), spontaneous motor activity reduces significantly with time. It gives an F-value of 3.818, which provides a p-value of (0.019) less than the significant level of 0.01. At the same time, the reduction in spontaneous motor activity has no significance between the groups. In TG2(X), spontaneous motor activity reduces significantly with time. It gives an F-value of 12.26, a p-value less than the significant level of 0.001. Here, the reduction between the groups is comparatively lower, with an F-value of 4.043, which gives a p-value less than the substantial level of 0.05. In TG3(2X), spontaneous motor activity reduces gradually, and the maximum reduction was attained at +120 min. For TG3(2X), the F-value calculated within the group is 6.395, which gives a p-value less than the significance level of 0.001. The reduction of spontaneous motor activity has no statistical significance between the groups. (Table 2)
On the 14th day, reduction in spontaneous motor activity within time in both sexes of mice had no significance in Group A (Control).

In TG1(1/2X), the reduction of spontaneous motor activity was gradual in both sexes of mice. The males attained maximum reduction at +60 min and, after that, slightly decreased at +90 min and +120 min, whereas females had a gradual reduction, and the maximum reduction was at +120 min. It gives an F-value within the female group as 7.942, with a p-value (0.007) significant at a level less than 0.01, whereas in males, the reduction has no statistical significance.

In TG2(X), both sexes of mice got a gradual reduction of spontaneous motor activity and attained a maximum decrease at +120 min. It gives an F-value of 6.303 for females, which provides a p-value with (0.014) significance at a level less than 0.05. In males, the calculated F-value is 12.63, which gives a p-value (0.002) significant at a level less than 0.01. In TG3, the reduction of spontaneous motor activity in males and females forms a steep straight line and co-inside each other at +90 min. Each sex of mice attains maximum reduction at +120 min. It gives an F-value of 20.03(0.000) for females, with a p-value significant at the level less than 0.001. In males, the calculated F-value is 6.742, which gives a p-value (0.011) significant at a level less than 0.05.

On the 14th day, the reduction in spontaneous motor activity within and between groups has no significance for Group A. In TG1(1/2X), spontaneous motor activity reduces significantly with time. It gives an F-value of 6.003, a p-value less than the significant level of 0.01. At the same time, the reduction in spontaneous motor activity has no significance between the groups. In TG2(X), spontaneous motor activity reduces significantly with time. It gives an F-value of 11.47, a p-value less than the significant level of 0.001. Here also, the reduction between the groups has no statistical significance. In TG3(2X), spontaneous motor activity reduces gradually, and the maximum reduction was attained at +120 min. For TG3(2X), the F-value calculated within the group is 25.90, which gives a p-value less than the significance level of 0.001. The reduction of spontaneous motor activity has no statistical significance between the groups. (Table 3)

DISCUSSION

The depressant action of drugs on CNS is mediated through both neural and hormonal mechanisms. The immediate reduction in spontaneous motor activity was achieved through the neural mechanism, and the prolonged effect was achieved through the hormonal action. The drug possesses bitter principles. The functional bitter taste is expressed in brain cells by bitter taste receptors T2R's. T2R-4, T2R-107, and T2R-38 transcripts are found in the brain stem, cerebral cortex and cerebellum. The drug is also a potent source of phytoestrogen, which has oestrogen-mimicking action.[6]

Beyond the primary endocrine and reproductive functions, oestrogen has significant actions in the CNS. It is often referred to as "nature's psycho-protectant". Oestrogen receptors can be abundant in multiple extra-hypothalamic regions throughout the brain, particularly the limbic system, basal ganglia, cerebellum and many areas of the cerebral cortex. Through classical genomic and non-genomic interactions with these receptors, oestrogen will function as a neuroactive steroid. It influences the signalling pathways with its neuro-modulatory functions. It has a significant effect on dopaminergic and serotonergic systems. The impact of oestrogen on the dopaminergic system is yet to be explored at the molecular level.[7]

The primary data on the serotonergic systems has concluded that the active form of oestrogen – oestradiol decreases the activity of monoamine oxidase, increases the activity of tryptophan hydroxylase, manipulates expression of the serotonin transporter, downregulates 5-HT1A receptors and upregulates 5-HT2A receptors. Thus, it reduces the signal transmission intensity in the motor neuron pathway. As the intensity of signal transmission gets reduced, the intensity of motor response also gets diminished and exhibits CNS depressant activity.[8]

CONCLUSION

In the CNS depressant activity study, the drug significantly reduces spontaneous motor activity on all assessment days, with a p-value<0.001. The drug enhances the depressant action in males at an effective dose in the first administration itself, whereas in females, the corresponding response is found with double doses. On prolonged administration for a week, depressant action was found to be maximum in females in a dose-dependent manner, *i.e.,* maximum inhibition occurred for the group treated with a double dose with a p-value<0.001. Also, this reduction is significant when compared with males with a p-value<0.05. After continuing the drug administration for two weeks, a similar reduction occurs both in males and females.

REFERENCES

1. Sharma RK and Dash B. Charaka Samhita: English translation and critical exposition based on Chakrapanidatta's Ayurvedadipika. Chaukhamba Sanskrit Series, Varanasi, 2014 Vol 1: p.100.
2. Pandit Haragovinda Sastri. Editor, Amarakosham of Amarasimha with Ramasrami Commentary of Bhanuji Dikshita, Reprint 2012, Varanasi, Chaukhamba Sanskrit Series, 2nd kandham, Vanoushadhi varga, p 202.
3. Joshi G Nirmala. Ayurvedic Concepts in Gynaecology, 2nd reprint, 2013, Varanasi, Chaukhamba Sanskriti Pratisthan, Dysmenorrhea, p 57.
4. Prabhakara Rao. Sharangdhara Samhita, Chaukhamba publications, New Delhi, 2015, p 78.
5. Hans Gerhard Vogel, Editor, Drug Discovery and Evaluation: Pharmacological Assays, 3rd Edition, Springer, 2018, p 634.

6. Chan GH and Fiscus RR. Exaggerated production of nitric oxide (NO) and increases in inducible NO –synthase mRNA levels induced by the proinflammatory cytokine interleukin-beta in vascular smooth muscle cells of elderly rats. Exp. Gerontol, 2004;3:387–394
7. Emiley Hayes *et al.* The role of oestrogen and other hormones in the Pathophysiology and Treatment of Schizophrenia, www.ncbi.nlm.nih.gov, 2012; 2012: 540273, PMID: 22966438.
8. Dr Praveen Balakrishnan, Author, Rasabhediyam, Kottakkal, Arya Vaidya Sala, Kottakkal Ayurveda Series:124, 2020, p 77.

Cite this article as:

Asha S Raj and Sara Monsy Oommen. CNS depressant activity of Kashaya of Asoka – *Saraca asoca* Roxb. De (Wilde.). Int. J. Res. Ayurveda Pharm. 2024;15(1):56-60
DOI: http://dx.doi.org/10.7897/2277-4343.15113

Source of support: Nil, Conflict of interest: None Declared