NATURE'S SHIELD: UNVEILING THE PROTECTIVE POWER OF SHARKARA YUKTA GAU-DUGDHA AS PRATIVISHA AGAINST DATURA METEL INDUCED TOXICITY IN ALBINO WISTAR RATS - A RESEARCH ARTICLE

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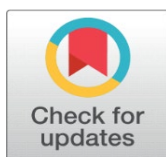
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ABSTRACT

Datura (Datura metel) is recognized as a cerebrotoxic deliriant poison and is concurrently categorized as "*Upavisha*" within *Ayurvedic* principles. *Ayurveda* encompasses a spectrum of toxic substances along with their respective antidotes; however, the mechanisms underlying these antidotal effects remain unelaborated in the ancient texts. A segment in the "*Rasa jal Nidhi*" Part 3 (Chapter 8), titled "*Dhusturbeejasya Shanti*," delineates the potential antidote properties of *Gau dugdha* in a proportion of *one prastha* and *sharkara* (sugar) in a quantity of *two pal*, positing a potential counteraction against *Datura* toxicity. The objective of this study is to scientifically evaluate the efficacy of these antidotal agents in mitigating *Datura* seed-induced toxicity, so that it can be useful in emergencies. Methods: Albino Wistar rats are employed as the chosen animal model to investigate the antidotal effect of *Sharkara Yuka Gau-dugdha* against *Datura beeja* (seed) powder-induced toxicity. The assessment encompasses a comprehensive range of criteria encompassing alterations in weight, modifications in dietary and hydration habits, behavioral shifts, lethaginss, fluctuations in temperature, emergence of convulsive episodes, performance in the Radial Arm Test, Rotarod activity, locomotion, and mortality. Results: Following administration of *Sharkara Yuka Gau-dugdha*, discernible alleviation of the deleterious effects associated with *Datura* exposure is evident. Noteworthy observations encompass a reduction in responses during the Radial Arm Test, suggestive of a positive influence on cognitive faculties such as learning and memory. Additionally, an increase in time spent on the Rotarod apparatus signifies enhanced muscle strength and augmented motor function. Conclusion: The findings gleaned from this experimental study culminate in the conclusion that *Sharkara Yuka Gau-dugdha* holds moderate potential to ameliorate the extent of toxic manifestations elicited by *Datura* exposure.

Keywords: *Datura, Sharkara, Gau- Dugdha, Agad,* Toxicity, Antidote

1. INTRODUCTION

In antiquity, *Ayurveda* held a preeminent status as an advanced field of knowledge. Within its realm, "*Agad tantra*" pertains to the branch that addresses

the toxic effects of various creatures such as snakes, spiders, insects, and rodents, along with their corresponding treatments. The term "*Gada*" signifies poison, and the counteragents employed are termed "*Agada*." In contemporary toxicology, the discipline engages in the comprehensive study of toxins, encompassing their origins, properties, modes of action, resulting symptoms, lethal doses, fatal intervals, and approaches to detection, quantification, and post-mortem findings. *Datura* (*Datura metel*), classified as cerebrotoxic and deliriant, is acknowledged within the *Ayurvedic* canon as an "*Upavisha*." This genus comprises toxic herbs and shrubs that attain heights of 3-4 feet. Notable for their intoxicating and narcotic attributes, these plants induce temporary insensibility in moderate doses, eliciting stupefying effects. *Datura metel*, commonly known as Devil's Trumpet or Angel's Trumpet, is a fascinating and enigmatic plant that has captured human fascination for centuries. Belonging to the Solanaceae family, this flowering plant is renowned for its striking and trumpet-shaped blossoms, which exude an alluring fragrance in the twilight hours. Throughout history, *Datura metel* has played a significant role in various cultures and societies. Its ethereal appearance, coupled with its potent psychoactive properties, has led to a myriad of religious, spiritual, and medicinal applications. However, it's important to note that *Datura metel* is a highly toxic plant and should be handled with extreme caution. *Datura metel*, along with other species in the *Datura* genus, is renowned for its extreme toxicity. The plant contains a cocktail of potent alkaloids, including atropine, scopolamine, and hyoscyamine, which are responsible for its psychoactive effects as well as its danger to human health. These tropane alkaloids act as competitive antagonists of acetylcholine receptors in the nervous system, leading to a wide range of physiological and psychological effects. Ingestion of any part of the *Datura metel* plant can have severe consequences, and even small amounts of the plant can be lethal. The toxicity levels can vary between different plant parts and growth stages, with the seeds, flowers, and leaves often carrying the highest concentration of alkaloids. Symptoms of *Datura* toxicity usually appear within 30 minutes to a few hours after ingestion and can last for several days. The effects are highly unpredictable and may vary from person to person. One of the most distinctive effects of *Datura* toxicity is vivid and often terrifying hallucinations. These hallucinations can be auditory, visual, or tactile, leading to confusion and disorientation. *Datura* poisoning can induce a state of extreme delirium, making it challenging for the affected individual to distinguish between reality and hallucinations. *Datura* alkaloids disrupt the autonomic nervous system, leading to dry mouth, dilated pupils, and blurred vision. The tropane alkaloids in *Datura* can cause tachycardia (increased heart rate), which can be particularly dangerous for individuals with pre-existing heart conditions. *Datura* toxicity can result in a loss of motor coordination, making simple tasks difficult and potentially leading to accidents. In severe cases, *Datura* poisoning may trigger seizures, posing a significant risk to the individual's health and safety. In extreme cases or when consumed in high doses, *Datura* toxicity can lead to a coma and even death due to respiratory failure or cardiac arrest. It's important to note that intentional use of *Datura* for its hallucinogenic effects is not only illegal but also extremely dangerous. The risk of overdose and unpredictable reactions make it a highly risky choice for recreational purposes. Additionally, accidental poisoning can occur, especially in children or individuals unaware of the plant's toxicity. Various poisons have been described in *Ayurveda* 6-8 along with their antidotes. These antidotes are readily available in nature. Mode of action of these antidotes is not mentioned in texts. In *Ayurvedic* literature according to *Ras jal nidhi* part 3 (chaptar 8) under the heading of *dusturbeejasya shanti*, *Gau dugdha*-one *prastha* and *sharkara*-2 *pal* has been

described to be possessing antidote action which may act by some way to counter toxicity of *Datura*.9-11 The properties of *gau dugdha*, according to *Ayurveda* are *Madhura, Sheeta, Mridu, Snigdha, Bahal, Slakshana, Picchila*, *Guru, Manda, Prasanna, Ojovardhaka* and *Pravara Jivaniya*. Thus, properties of the milk are similar to *Ojas* i.e, promoting immunity or body defense mechanism. The properties of *Ojas* are opposite to *Visha. Sharkara* contains *madhura rasa, snigdha guna, sita virya and madhura vipaka. Sharkara is chaksusya, dhatu vardhaka, hridya, pittahara, vatahara and vrisya. Sharkara* pacifies *vata, pitta, rakta dosha* and cures the symptoms caused by unconsiousness, vomiting and poison intake. Main chemical constituents of *Gau-dugdha* are Protein (3.2%), Fat (3.9%), Carbohydrates i.e. Lactose (4.9%), Mineral compounds (0.90%), Water (87%), trace of Amino acids (101.7mg/litre), Minerals, Enzymes, Vitamins, Calories-65% and *sharkara* are Energy: 1,619 kJ (387 kcal), Water: 0.03 g, Iron: 0.01 mg, Carbohydrates: 99.98 g, Riboflavin (Vit. B$_2$): 0.019 mg (2%), Calcium: 1 mg, Sugars: 99.91 g. It is necessary to verify the efficacy of these antidotes on scientific parameters15 so that it can be useful in emergencies. Hence present study entitled "*Sharkara Yukta Gau-dugdha* as an Antidote in *Datura* poisoning in albino wistar rats, was carried out to establish the action and mechanism of *Sharkara Yukta Gau-dugdha* against toxic effects of *Datura* on albino wistar rats. Acharya (2000)

2. MATERIAL AND METHODS
2.1. DRUG IDENTIFICATION AND AUTHENTICATION

The sample of raw drugs were authenticated by expert of *Dravyaguna* department U.A.U. Rishikul campus, Haridwar.

2.2. COLLECTION OF DRUGS

- **Date of collection (*Datura* fruits) -** June 2022

Fresh *Datura* fruits were collected from Herbal garden, Shyampur, Nazibabad road, Haridwar. Fruits were dried in sunlight and seeds were collected for the study. *Gau dugdha* and *Sharkara* were collected from the authentic sources.

- **Drug Preparation-**

Coarse powder of *Datura* seeds was prepared by grinding and mixed with 1% CMC solution.

Animal Experiment Material for In Vivo study Albino wistar rats of age 8-12 weeks and weight ranges 100-250 gm were procured. Poisoning was induced by *Datura* seeds and test drug was *Gau dugdha* and *Sharkara*.

Determination of acute toxicity of *Datura* seeds is performed as per guideline of OECD 423 in Albino wistar rats.

Determination of protective action of *Sharkara Yukta Gau-dugdha* against toxicity of *Datura* seed Reduction in mortality and change in behaviour of rats due to a lethal dose of *Datura* seed after administration of *Sharkara Yukta Gau-dugdha* are determined.

2.3. STUDY DESIGN

1) Animal Sources:

- Healthy rats were selected for experimentation.
- Animals were maintained as per Animal Ethical Committee regulations.
- Experimental protocol was approved from IAEC (Institutional Animal Ethics Committee) and whole experiment was performed under the guidelines of CPCSEA (Committee for Purpose of Control and Supervision of Experimental on Animals).

2) Inclusion criteria-

Healthy Female wistar rats weighing between 100-250 grams.

3) Exclusion criteria-

Unhealthy rats were discarded.

The rats were discarded, if the weight is not within ±20% of the mean initial weight.

The parous and the pregnant female rats were discarded.

Rats which were under trial of other experiment.

Table 1

Table 1 Showing Animal Experiment Groups				
S. No.	GROUPS	GROUP NAME	TREAMENT	ANIMALS
1.	Group 1	Control Group	No treatment	6
2.	Group 2	Acute Poisoning Group	Oral administration of powder of *datura* seeds	6
3.	Group 3	Study Group	*Sharkra yukta Gau–dugdha* after administration of *datura* seeds	6

4) **Housing and feeding conditions-** The temperature in the experimental animal room had been 22^{0}C (**±3^{0}C**). Although the relative humidity had been at least 30% and preferably not exceed the sequence being 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water.

5) **Oral Acute Toxicity study-:**

The antidote study was performed as per **OECD423 guideline-**

Animal species used   -   Wister rats

Sex of animal   -   Female

Age of animal   -   8-12 weeks

Average weight of animal   -   100-250 gm

Total no. of animals   -   18

No. of groups   -   3

No. of animal in each group -   6

Period of fasting   -   Over night

Feeding   -   Standard palatable diet

Water   -   R.o. drinking water

Temperature   -   22±3°C

Humidity   -   30-70%

Vehicle   -   CMC solution

Route   -   Oral

Experimental drug   -   *Datura beeja* (seed)

Antidotal drug   -   *Sharkara yukta gau-dugdha*

Observation period - 14 days

6) Preparation of animals-

The animals are randomly selected, marked with Picric acid, H (mark on head), B (Mark on Back), T (mark on Tail) for individual identification, and kept in their cages for at least 5 days prior to dosing to allow for acclimatisation to the laboratory conditions.

7) Number of animals and dose levels-

Eighteen albino wistar rats had been divided in three groups. Each group contain 6 wistar rats as follows-

Group 1 had six wistar rats and they had received CMC (1%) solution 5ml/kg/P.O in a single dose.

Group 2 had six wistar rats and they had received *Datura beej* (seed) *churna* 111mg/ kg/P.O (10%) in a single dose along with C.M.C. solution.

Group 3 had six wistar rats and they had received *Sharkara yukta gau-dugdha* (8.9:1.1)   10ml/kg   orally   after   inducing   poisoning by *Daturabeej* (seed) *churna* 111mg/ kg/P.O (10%) in a single dose.

Dose was administered orally in a single dose by gavage.

Dose was calculated according to their body weight.

Dose was decided on the basis of **Pagets & Brane's rule, 1964 i.e. (0.018× human dose ×5).**

Following the period of fasting, the animals were weighed and the test substance administered.

After the substance had been administered, food was withheld for a further 3-4 hours in rats.

Dose Calculation for Albino wistar rats the conversion factor from man to rats is 0.018 so according to this, all the doses were calculated. Dose for rats was obtained from the following formula Dose of rats = 0.018 × human dose × 5.

Dose Calculation for *Datura* Seeds, Human fatal Dose for *Datura* Seeds is considered as 120 crushed seeds i.e. calculated as 1234 mg. According to the conversion factor, fatal dose in albino wistar rats for *Datura* is 111 mg Hence per kg wt. Fatal dose for albino wistar rats = 0.018 x 1234 x 5 = 111 mg/kg.

Dose Calculation for *Sharkara Yukta Gau-dugdha:* Human therapeutic dose of *Gau-dugdha* and *Sharkara* is considered as 768 gm and 96 gm. The ratio of *Gau-dugdha* and *Sharkara* for albino wistar rats is 8.9:1.1. Dose Calculation for *Sharkara Yukta Gau-dugdha*, according to the wt. of albino wistar rats is 10ml/kg.

Table 2

Table 2 Showing Dosing Chart of Group 1		
Group 1		
Marking	**Weight (gm)**	**CMC Sol 5 ml/ kg (ml)**
H	200	1
B	195	0.975
T	145	0.725
HB	196	0.98
BT	180	0.9
HT	172	0.86

Table 3

Table 3 Showing Dosing Chart of Group 2		
Group 2		
Marking	**Weight (gm)**	**Dhatura seeds 111 mg/ kg (10 %)**
		Dose in mg	**Dose in ml**
H	171	18.981	0.19
B	196	21.756	0.22
T	174	19.314	0.19
HB	217	24.087	0.24
BT	165	18.315	0.18
HT	152	16.872	0.17

Table 4

Table 4 Showing Dosing Chart of Group 3				
Group 3				
Marking	**Weight (gm)**	**Dhatura seeds 111 mg/ kg (10 %)**		**Cow milk + suger (8.9:1.1) 5 ml/kg**
		Dose in mg	**Dose in ml**	**Dose in ml**
H	**134**	14.874	0.15	0.67
B	**180**	19.98	0.20	0.9
T	**190**	21.09	0.21	0.95
HB	**213**	23.643	0.24	1.065
BT	**220**	24.42	0.24	1.1
HT	**193**	21.423	0.21	0.965

8) **Observations-** Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days.

All observations were systematically recorded with individual records being maintained for each animal.

Observations include changes in skin and fur, eyes, mucous membranes, salivation, Lethargy, sleep, coma, convulsions, tremors, diarrohea, morbidity, mortality, water and food intake, rectal temperature, Learning memory observation on radial arm maze was observed.

3. ASSESMENT CRITERIA

The assessment criteria of antidotal effect of *Sharkara yukta Gau-dughdha* were made on the basis of-
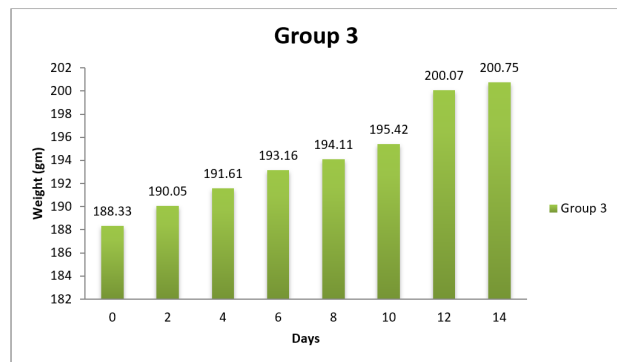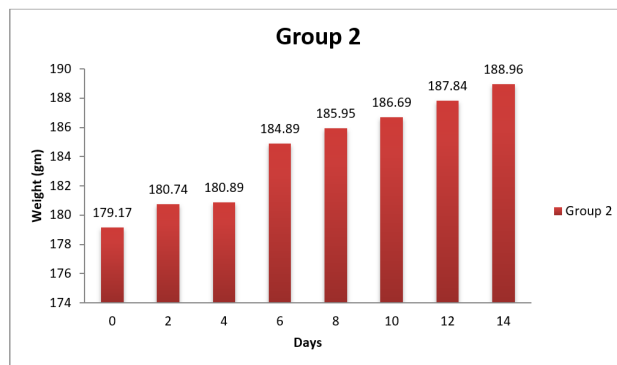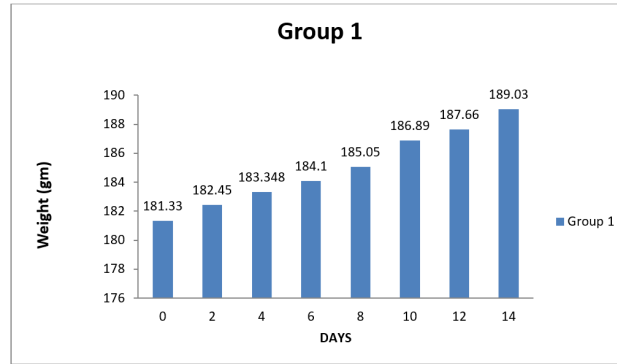
- Weight changes
- Changes in food and water habits
- Behaviour changes-Salivation, Urination
- Change in temperature
- Appearance of Convulsion
- Radial Arm Test
- Rotarod Test
- Mobility & Mortality

4. RESULTS AND DISCUSSION

The results are expressed as Mean ± SEM Comparison between each group were performed by analysis of variance (ANOVA) with Dunnett's 't' test for determining the level of significance. P value less than 0.05 was considered as statistically significant. Acharya (2012)

Table 5

Weight (gm)	Group 1		Group 2		Group 3	
	Mean±SEM	No	Mean±SEM	No	Mean±SEM	No
0 day	181.33±8.48	6	179.17±9.57	6	188.33±12.46	6
8 day	185.05±8.44	6	185.95±12.34	5	194.11±12.43	6
14day	189.03±8.34	6	188.96±12.14	5	200.75±12.91	6

Table 5 Showing Statistical Analysis of Weight Changes

4.1. RESULT OF WEIGHT CHANGES

Table 6

Table 6 Showing Comparison Between Weight (gm) Changes of all groups

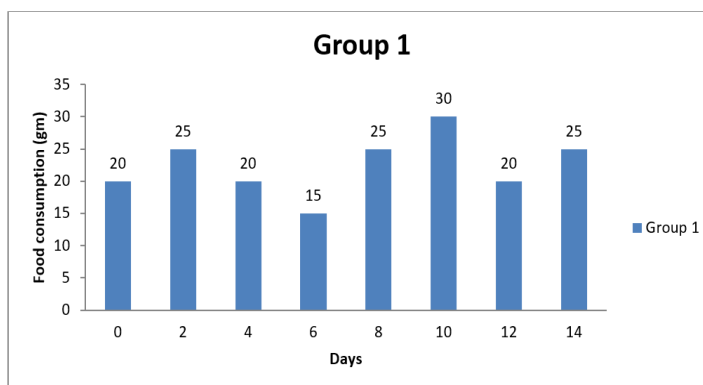| Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Adjusted P Value
0 day:Group 1 vs. 0 day:Group 2	2.160	-42.95 to 47.27	No	0.9998
0 day:Group 1 vs. 0 day:Group 3	-7.000	-52.11 to 38.11	No	0.9994

|				
0 day:Group 1 vs. 8 day:Group 1	-3.720	-48.83 to 41.39	No	0.9997
0 day:Group 1 vs. 8 day:Group 2	-4.620	-51.93 to 42.69	No	0.9996
0 day:Group 1 vs. 8 day:Group 3	-12.78	-57.89 to 32.33	No	0.9949
0 day:Group 1 vs. 14day:Group 1	-7.700	-52.81 to 37.41	No	0.9993
0 day:Group 1 vs. 14day:Group 2	-7.630	-54.94 to 39.68	No	0.9993
0 day:Group 1 vs. 14day:Group 3	-19.42	-64.53 to 25.69	No	0.9263

There were no significant differences observed between the weight changes of Group 1 and the other groups at various time points (0 day, 8 day, and 14 day). The mean differences in weight changes between Group 1 and the other groups were relatively small and not statistically significant, as evidenced by the wide 95.00% confidence intervals that include zero. The adjusted p-values for all comparisons were close to 1, indicating that the differences observed were likely due to chance rather than meaningful effects. Therefore, based on this analysis, there were no significant differences in weight changes between the groups during the study period. Paradakara (2011)

Table 7

Table 7 Showing Statistical Analysis of Food Consumption					
Food consumption (gm)	Group 1		Group 2		Group 3
	Mean± SEM	No	Mean±SEM	No	Mean±SEM	No
0 day	20±0.00	6	20±0.00	6	15±0.00	6
8 day	25±0.00	6	20±0.00	5	15±0.00	6
14day	25±0.00	6	20±0.00	5	25±0.00	6
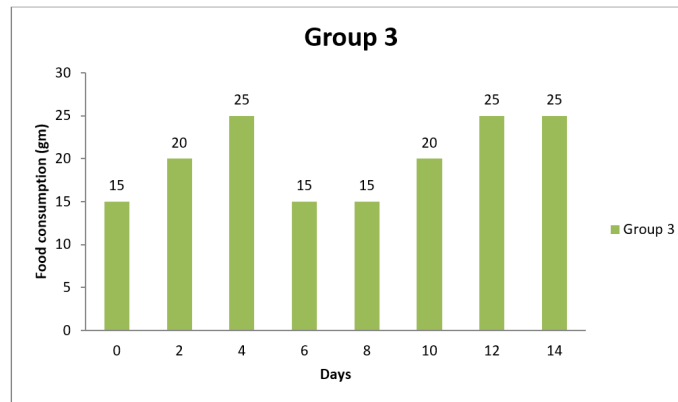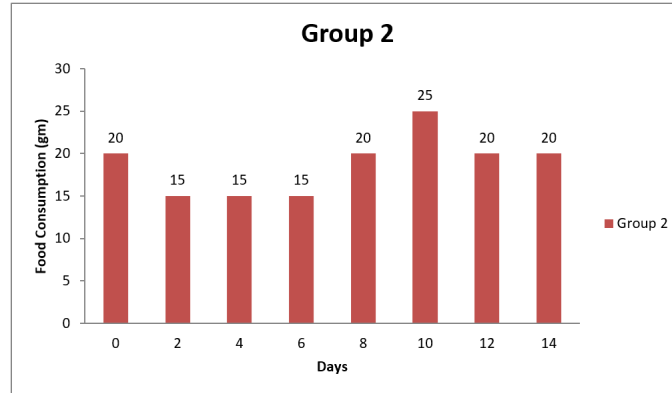
4.2. RESULT OF FOOD CONSUMPTION

Table 8

Table 8 Showing Comparison Between Food Consumption of all Groups				
Dunnett's multiple comparisons test	**Mean Diff.**	**95.00% CI of diff.**	**Significant?**	**Adjusted P Value**
0 day:Group 1 vs. 0 day:Group 2	15.35	15.35 to 15.35	Yes	<0.0001
0 day:Group 1 vs. 0 day:Group 3	5.000	5.000 to 5.000	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 1	-5.000	-5.000 to -5.000	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 2	15.44	15.44 to 15.44	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 3	5.000	5.000 to 5.000	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 1	-5.000	-5.000 to -5.000	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 2	13.15	13.15 to 13.15	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 3	-5.000	-5.000 to -5.000	Yes	<0.0001

Significant differences were observed in food consumption between Group 1 and the other groups at various time points (0 day, 8 day, and 14 day). The mean differences in food consumption between Group 1 and the other groups were statistically significant, as evidenced by the narrow 95.00% confidence intervals that do not include zero. The adjusted p-values for all comparisons were very small (less than 0.0001), indicating strong evidence of significant differences in food consumption between the groups during the study period. Specifically, Group 1 showed higher food consumption than Groups 2 and 3 at 0 day and 8 day, as indicated by positive mean differences. Conversely, at 8 day and 14 day, Group 1 had

lower food consumption than Groups 1, 2, and 3, as indicated by negative mean differences. Overall, this analysis suggests that there are significant differences in food consumption between the groups, with Group 1 exhibiting distinct patterns of food intake compared to the other groups throughout the study duration.

Table 9

Table 9 Showing Statistical Analysis of Water Consumption						
Water consumption (ml)	Group 1		Group 2		Group 3	
	Mean±SEM	No	Mean±SEM	No	Mean±SEM	No
0 day	4.56±0.00	6	4.65±0.00	6	5.69±0.00	6
8 day	4.85±0.00	6	4.56±0.00	5	6.69±0.00	6
14day	5.93±0.00	6	6.85±0.00	5	6.19±0.00	6
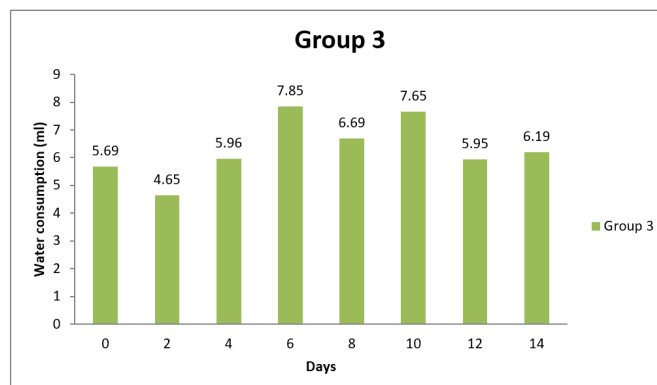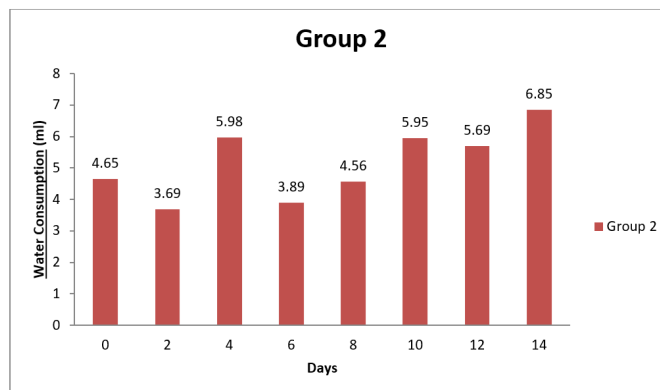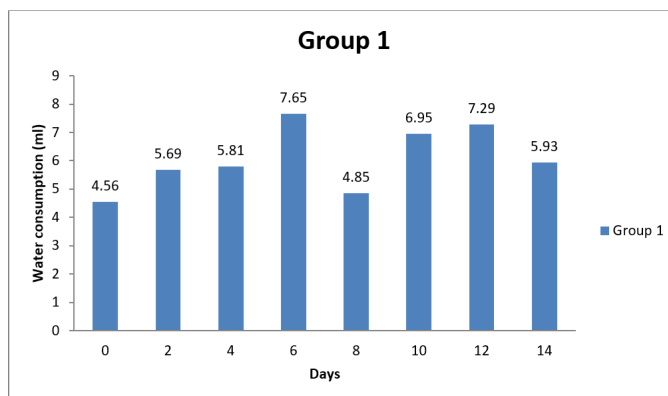
4.3. RESULT OF WATER CONSUMPTION

Table 10

Table 10 Showing Comparison Between Water Consumption (ml) of all Groups				
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Adjusted P Value
0 day:Group 1 vs. 0 day:Group 2	-15.44	-15.44 to -15.44	Yes	<0.0001
0 day:Group 1 vs. 0 day:Group 3	-1.130	-1.130 to -1.130	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 1	-0.2900	-0.2900 to -0.2900	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 2	-15.44	-15.44 to -15.44	Yes	<0.0001
0 day:Group 1 vs. 8 day:Group 3	-2.130	-2.130 to -2.130	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 1	-1.370	-1.370 to -1.370	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 2	-15.44	-15.44 to -15.44	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 3	-1.630	-1.630 to -1.630	Yes	<0.0001

Significant differences were observed in water consumption between Group 1 and the other groups at various time points (0 day, 8 day, and 14 day). The mean differences in water consumption between Group 1 and the other groups were statistically significant, as evidenced by the narrow 95.00% confidence intervals that do not include zero. The adjusted p-values for all comparisons were very small (less than 0.0001), indicating strong evidence of significant differences in water consumption between the groups during the study period. Specifically, Group 1 showed lower water consumption compared to Groups 2 and 3 at 0 day and 8 day, as indicated by negative mean differences. Similarly, at 8 day and 14 day, Group 1 had lower water consumption than Groups 1, 2, and 3, as indicated by negative mean differences. Overall, this analysis suggests that there are significant differences in water consumption between the groups, with Group 1 consistently exhibiting lower water intake compared to the other groups throughout the study duration.

Table 11

Table 11 Showing Statistical Analysis of Rotarod Test					
Rotarod (Sec)	Group 1		Group 2		Group 3	
	Mean±SEM	No	Mean±SEM	No	Mean±SEM	No
0 day	9.53±1.13	6	6.09±1.55	6	6.11±0.71	6
8 day	12.98±1.39	6	8.02±0.65	5	11.26±1.26	6
14day	17.49±1.41	6	8.09±0.77	5	15.06±0.95	6
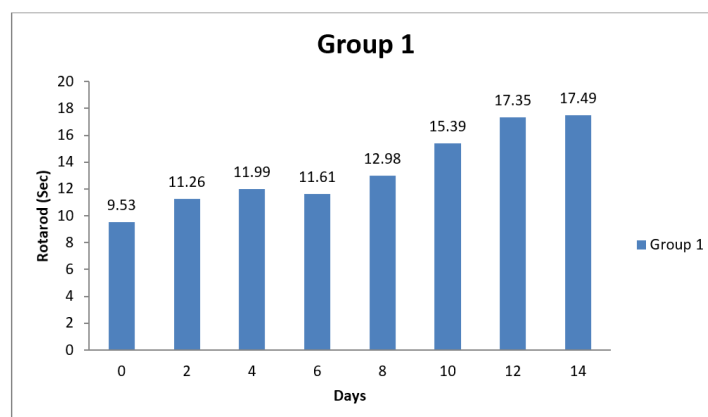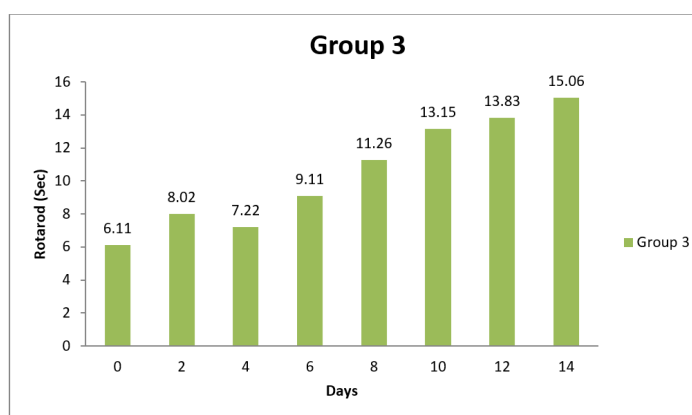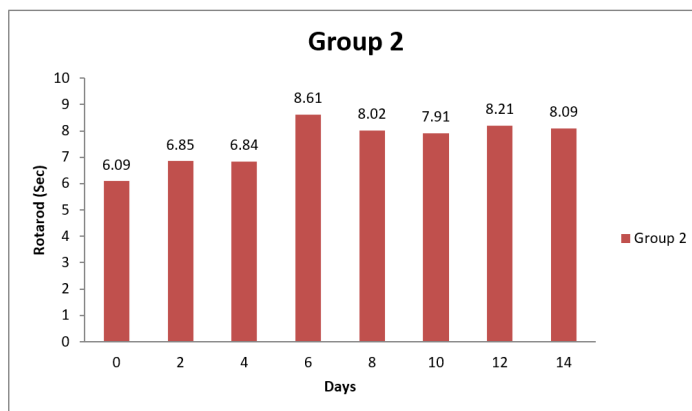
4.4. RESULT OF ROTAROD
Table 12

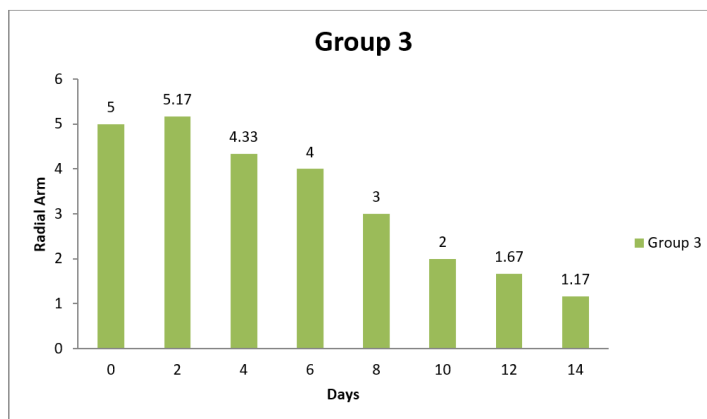| Table 12 Showing Comparison Between Rotarod (Sec) Test of all Groups				
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Adjusted P Value
0 day:Group 1 vs. 0 day:Group 2	3.440	-1.340 to 8.220	No	0.3286
0 day:Group 1 vs. 0 day:Group 3	3.420	-1.360 to 8.200	No	0.3362
0 day:Group 1 vs. 8 day:Group 1	-3.450	-8.230 to 1.330	No	0.3250
0 day:Group 1 vs. 8 day:Group 2	1.510	-3.503 to 6.523	No	0.9944
0 day:Group 1 vs. 8 day:Group 3	-1.730	-6.510 to 3.050	No	0.9842
0 day:Group 1 vs. 14day:Group 1	-7.960	-12.74 to -3.180	Yes	<0.0001
0 day:Group 1 vs. 14day:Group 2	1.440	-3.573 to 6.453	No	0.9948
0 day:Group 1 vs. 14day:Group 3	-5.530	-10.31 to 0.7503	Yes	0.0129

There were significant differences observed in the Rotarod test performance between Group 1 and some of the other groups at certain time points (0 day, 8 day, and 14 day). The mean differences in Rotarod test results between Group 1 and the other groups were statistically significant in two instances, as evidenced by the narrow 95.00% confidence intervals and the adjusted p-values less than 0.05. Specifically, at 14 day, Group 1 had significantly lower performance in the Rotarod test compared to Group 1 and Group 3, as indicated by negative mean differences. Conversely, there were no significant differences in Rotarod test performance between Group 1 and the other groups at 0 day and 8 day, as indicated by the wide confidence intervals that include zero and the adjusted p-values greater than 0.05. In conclusion, this analysis suggests that there were no significant differences in Rotarod test performance between Group 1 and most of the other groups at the initial time points (0 day and 8 day). However, at 14 day, Group 1 exhibited significantly lower performance in the Rotarod test compared to some of the other groups. Shastri (2001)

Table 13

Table 13 Showing Statistical Analysis of Radial Arm Test						
Radial Arm	Group 1		Group 2		Group 3	
	Mean±SEM	No	Mean±SEM	No	Mean±SEM	No
0 day	5.83±1.99	6	5.83±1.14	6	5.00±1.79	6
8 day	3.00±1.03	6	5.80±0.58	5	3.00±0.58	6
14day	1.17±0.17	6	3.60±0.81	5	1.17±0.17	6
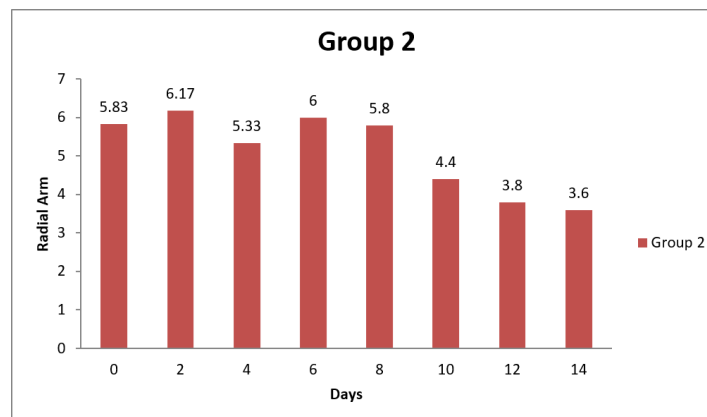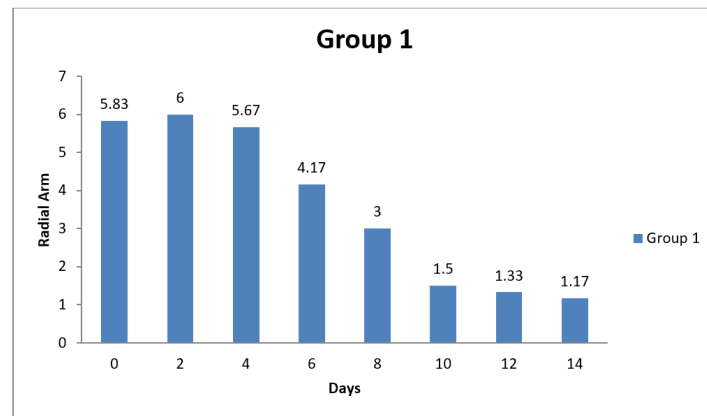
4.5. RESULT OF RADIAL ARM

Table 14

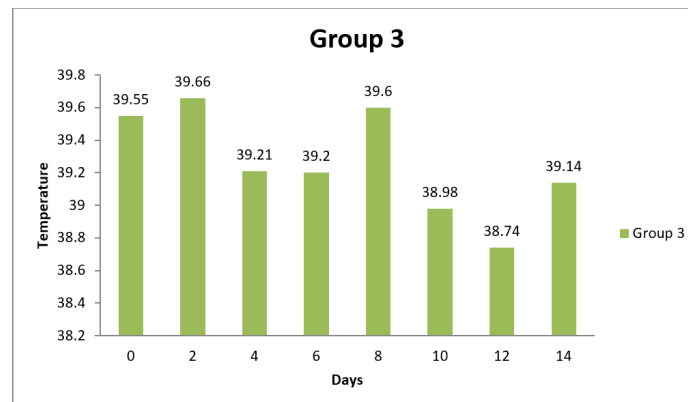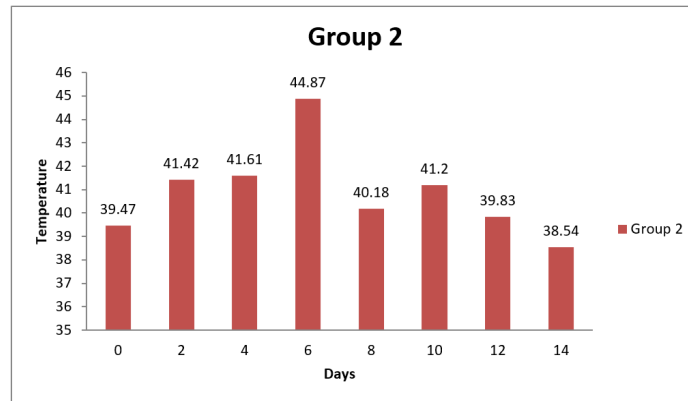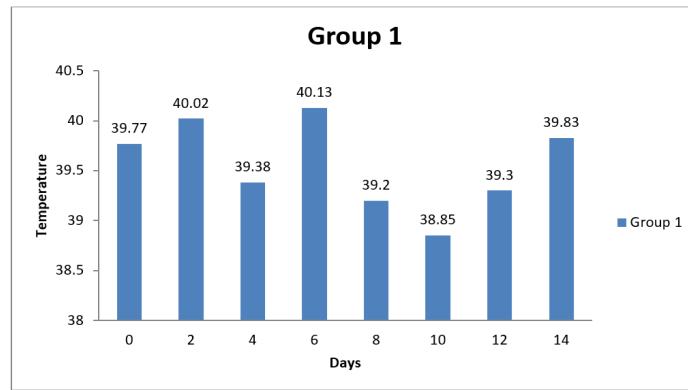| Table 14 Showing Comparison Between Radial Arm Test of all Groups				
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Adjusted P Value
0 day:Group 1 vs. 0 day:Group 2	0.000	-4.503 to 4.503	No	>0.9999
0 day:Group 1 vs. 0 day:Group 3	0.8300	-3.673 to 5.333	No	0.9992
0 day:Group 1 vs. 8 day:Group 1	2.830	-1.673 to 7.333	No	0.5137
0 day:Group 1 vs. 8 day:Group 2	0.03000	-4.692 to 4.752	No	>0.9999
0 day:Group 1 vs. 8 day:Group 3	2.830	-1.673 to 7.333	No	0.5137
0 day:Group 1 vs. 14day:Group 1	4.660	0.1575 to 9.163	Yes	0.0376
0 day:Group 1 vs. 14day:Group 2	2.230	-2.492 to 6.952	No	0.8620
0 day:Group 1 vs. 14day:Group 3	4.660	0.1575 to 9.163	Yes	0.0376

There were significant differences observed in the Radial Arm Test performance between Group 1 and one of the other groups at the 14-day time point. Additionally, there was a marginally significant difference at the same time point between Group 1 and another group. However, there were no significant differences in Radial Arm Test performance between Group 1 and the other groups at the initial time points (0 day and 8 day). Specifically, at 14 day, Group 1 showed significantly better performance in the Radial Arm Test compared to Group 1 and Group 3, as indicated by positive mean differences and adjusted p-values less than 0.05. Additionally, there was a marginally significant difference in Radial Arm Test performance between Group 1 and Group 3 at 14 day, as indicated by another positive mean difference and an adjusted p-value of 0.0376. In contrast, at 0 day and 8 day, there were no significant differences in Radial Arm Test performance between Group 1 and the other groups, as indicated by mean differences close to

zero and adjusted p-values greater than 0.05. In conclusion, this analysis suggests that Group 1 exhibited better performance in the Radial Arm Test compared to some of the other groups at the 14-day time point, while no significant differences were observed at the earlier time points (0 day and 8 day). Shastri (2011)

Table 15

Table 15 Showing Statistical Analysis of Temperature							
Temperature	**Group 1**		**Group 2**		**Group 3**	
	Mean±SEM	**No**	**Mean±SEM**	**No**	**Mean±SEM**	**No**
0 day	39.77±0.57	6	39.47±0.21	6	39.55±0.58	6
8 day	39.20±0.27	6	40.18±0.27	5	39.60±0.46	6
14day	39.83±0.21	6	38.54±1.69	5	39.14±0.35	6

4.6. RESULT OF TEMPERATURE

Table 16

Table 16 Showing Comparison Between Temperature of all Groups				
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Adjusted P Value
0 day:Group 1 vs. 0 day:Group 2	0.3000	-3.435 to 4.035	No	0.9997
0 day:Group 1 vs. 0 day:Group 3	0.2200	-3.515 to 3.955	No	0.9998
0 day:Group 1 vs. 8 day:Group 1	0.5700	-3.165 to 4.305	No	0.9994
0 day:Group 1 vs. 8 day:Group 2	-0.4100	-4.327 to 3.507	No	0.9996
0 day:Group 1 vs. 8 day:Group 3	0.1700	-3.565 to 3.905	No	0.9998
0 day:Group 1 vs. 14day:Group 1	-0.06000	-3.795 to 3.675	No	>0.9999
0 day:Group 1 vs. 14day:Group 2	1.230	-2.687 to 5.147	No	0.9940
0 day:Group 1 vs. 14day:Group 3	0.6300	-3.105 to 4.365	No	0.9993

There were no significant differences observed in the temperature measurements between Group 1 and any of the other groups at all time points (0 day, 8 day, and 14 day). The mean differences in temperature between Group 1 and the other groups were relatively small, and the 95.00% confidence intervals all included zero. Additionally, the adjusted p-values for all comparisons were close to 1, indicating that the observed differences in temperature were not statistically significant. In conclusion, based on this analysis, there were no significant differences in temperature measurements between Group 1 and the other groups during the entire study duration (0 day, 8 day, and 14 day). The temperature values for all groups appeared to be relatively similar and did not vary significantly from each other.

5. CONCLUSION

Datura, a neurotoxic cerebral deliriant poison, is also classified as "*Upavish*" in *Ayurveda*, characterized by its 9 distinct toxic effects. Its active compound, daturine, comprises hyoscine, hyoscyamine, and atropine. This compound functions by blocking acetylcholine receptors, leading to the manifestation of sympathomimetic or parasympatholytic actions, thereby inducing anticholinergic effects. Initial symptoms include a bitter taste, parched mouth and throat, gastric discomfort, dysphagia, cephalalgia, and dysphonia. These are subsequently followed by vertigo, an unsteady gait, impaired muscular coordination, a distinctive flushed facial appearance, xerotic and hyperthermic skin, photophobia, mydriasis, delirium, and somnolence. On occasion, widespread desquamation of the skin may become evident. The cardiac rhythm becomes irregular and sporadic. In instances of lethality, somnolence transitions to stupor, convulsive episodes ensue, eventually leading to coma, culminating in death, primarily due to respiratory insufficiency. In vivo study of Antidotal properties of *Sharkara Yukta Gau-Dugdha* shows, **In Group first** all behavioural parameter like Skin and Fur, Eyes, Mucous Membrane, Sleep was normal. Salivation, Lethargy, Coma, Convulsions, Tremors, Diarrhea, Morbidity, Mortality were absent. Changes in weight, food, water intake, rectal temperature, learning memory and muscle strength and motor activity were in normal range. **In Group second** all behavioural parameter like Skin and Fur, Eyes, Mucous Membrane, Sleep was normal. Salivation, Coma, Tremors were absent. Lethargy, Convulsions, Diarrhea was found in rats and Mortality in one rat was found. Changes

in weight was slightly decreased but it was statistically insignificant, food and water intake were slightly decreased but it was statistically significant and rectal temperature was increased in between 2nd to 10th day in toxicity group second but it was statistically insignificant. Response on radial arm was increased, it indicates that showing sample having negative effect on learning and memory and time spent on rota rod was decreased in comparison of group first and third but it was statistically insignificant, it indicates muscle strength and motor activity was decreased in toxicity group second. **In Group third** all behavioural parameter like Skin and Fur, Eyes, Mucous Membrane, Sleep was normal. Salivation, Lethargy, Coma, Convulsions, Tremors, Diarrhea, Morbidity, Mortality were absent. Changes in weight food water intake, rectal temperature was in normal range, response on radial arm was decreased that showing sample having positive effect on learning and memory and time spent on rota rod was increased in comparison of group 2nd, it indicate muscle strength and motor activity was increased in treatment group third but it was statistically insignificant. The in vivo study suggests that *Sharkara Yukta Gau-Dugdha* possesses moderate potential in mitigating *Datura metel* toxicity. The combination of *Gau-dugdha* and *Sharkara* might exhibits hepatoprotective, antioxidant properties, soothing effect and acts as a demulcent, thereby reducing the toxic effects of *Datura metel* alkaloids. *Datura metel* shares properties similar to *visha* (poisonous substances), while *Gau dugdha* (cow's milk) shares properties similar to *oja* (vital essence or immunity). In the classical texts, *Acharya Charak* mentioned that the properties of *oja* are opposite to *visha*, suggesting that *Gau dugdha's* properties may counteract the effects of *Datura metel* due to their opposing nature. According to *Dravyaguna Samgreh, Sharkara* (sugar) is believed to pacify *vata, pitta*, and *rakta dosha*. When it comes to counteract the effects of *visha* (poison). The probable mode of action of Sharkara could be, it contains *madhura rasa, snigdha guna, sheeta virya and madhura vipaka. Sharkara is chaksusya, dhatu vardhaka, hridya, pittahara, vatahara and vrisya* may help to balance and soothe the aggravated *vishad, vyavayi, vikasi* guna which are responsible for symptoms like hyperthermia caused by *visha*. Datura has deliriant properties and exerts anticholinergic effects. Manifestations of Datura toxicity within toxicity group 2, characterized by lethargy and diminished muscle tone, arise from acetylcholine receptor blockade. Convulsions ensue as neurons become hyperactive, resulting in uncontrolled electrical signaling. In this context, the selected antidote, "sharkara yukta gau-dugdha," appears to mitigate the aforementioned pathophysiological processes by rectifying neuronal dysfunction and counteracting the anticholinergic impact associated with Datura toxicity. Hence from this experimental study entitled "ROLE OF *SHARKARA YUKTA GAU-DUGDHA* AS *PRATIVISHA* IN *DATURA METEL* INDUCED TOXICITY- AN IN VIVO STUDY", it is clear that the *Sharkara yukta gau-dugdha* has moderate antidotal effect against *Datura* induced toxicity. From this study, we can conclude that *Sharkara yukta gau-dugdha* can reduce the toxic effects of *Datura* up to some extent. So, In this experimental study null hypothesis (H_o) is rejected and alternative hypothesis (H_1) is accepted up to some extent.

CONFLICT OF INTERESTS

None.

ACKNOWLEDGMENTS

None.

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