

## Anticonvulsant effect of *Rosa damascena* in pentylenetetrazole and maximal electroshock induced convulsions in albino rats

Hemapriya Tirupathi\*, Padmavathi Golla

Department of Pharmacology,  
Sri Padmavathi Medical College  
for Women, Tirupathi,  
Andhrapradesh, India

**Received:** 09 July 2016

**Accepted:** 09 August 2016

**\*Correspondence to:**

Dr. Hemapriya Tirupathi,  
Email: [hemapriyatirupathi@gmail.com](mailto:hemapriyatirupathi@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** *Rosa damascena mill L* (*Rosa damascena*) is an ornamental plant that has several therapeutic (such as sedative and hypnotic) effects. It also heals depression, grief, nervous stress and tension. In the present study we evaluated Anticonvulsant like effect of *Rosa damascena* in pentylenetetrazole (PTZ) and MES induced convulsions in albino rats.

**Methods:** MES model: rats were divided into 4 groups of 6 rats each. Group-I received 0.5% normal saline, group-II (standard) received phenytoin 25 mg/kg, group-III, IV received low dose (200 mg/kg) and high dose (400 mg/kg) of *rosa damascena* respectively orally convulsions were produced in all groups by giving maximum electric shock of 150 mA for 0.2 sec after 1 hour of giving test and standard drugs orally. Tonic clonic seizures were produced after giving electric shock .recovery time was noted. The percentage of inhibition of convulsions by drugs was measured and compared between the control, standard and test.

PTZ model: rats were divided and test drugs were given same as above model but standard drug was sodium valporate (200 mg/kg). Convulsions were induced by giving the pentylenetetrazole IP 1hour after giving test and standard drugs intra-peritonelly. The onset of convulsions, duration of action and type of seizures were noted and compared between standard and test groups.

**Results:** In MES Model, aqueous extract of *Rosa damascena* significantly ( $p < 0.001$ ) decreased the duration of tonic clonic seizures and recovery time. In PTZ model the onset of seizures was delayed ( $p < 0.001$ ) with low and high doses and the duration of convulsions was reduced effectively ( $p < 0.001$ ). Type of seizure was controlled in initial phase and number of seizures was also reduced.

**Conclusions:** *Rosa damascena* was shown anticonvulsant property in both MES and PTZ animal models.

**Keywords:** *Rosa damascena*, Rats, Phenytoin, Sodium valporate

### INTRODUCTION

*Rosa damascena mill L* (*Rosa damascena*), commonly known as Damask rose, is one of the most important species of *Rosaceae* family which is a well-known ornamental plant in the world that has been referred to as the king of flowers.<sup>1-3</sup>

The major cultivation areas of *Rosa damascena* in Iran are Kashan, Fars and Azerbaijan, among them Kashan is the most famous one.<sup>4</sup> The most therapeutic effects of *Rosa damascena* in ancient medicine are treatment of abdominal and chest pain, strengthening the heart, treatment of menstrual bleeding and digestive problems and reduction of inflammation, especially of the neck.<sup>5,6</sup>

North American Indian tribes used a decoction of the root of *Rosa damascena* plant as a cough remedy to ease children's cough.<sup>7</sup> This plant is also used as a gentle laxative.<sup>8</sup> Rose oil heals depression, grief, nervous stress and tension. It helps in the reduction of thirst, old cough, special complaints of women, wound healing, and skin health. Vapour therapy of rose oil is helpful for some allergies, headaches, and migraine.<sup>8,9</sup>

Several components were isolated from flowers, petals and hips (seed-pot) of *Rosa damascena* including terpenes, glycosides, flavonoids and anthocyanins. This plant contains carboxylic acid, myrcene, vitamin C, kaempferol and quercetin.<sup>10-16</sup> The essential oil of *Rosa damascena* in acute pentylenetetrazole (PTZ)-induced seizure in rats, delays the start of epileptic seizures and

decrease the duration of tonic-clonic seizures (stage 4). In chronic model of PTZ induced seizure, this plant also caused prolongation of latent periods before tonic clonic generalized seizures. It is also suggested that essential oil of *Rosa damascena* retarded the development of behavioural seizures in amygdale electrical kindling and possesses the ability to counteract kindling acquisition. The aqueous and ethanolic extracts of *Rosa damascena* have potentially anticonvulsant effect in PTZ induced seizure and MES model in mice.<sup>17-19</sup>

## METHODS

### *Plant material and preparation of extract of Rosa damascena*

Plants were collected from Nellore district, Andhra Pradesh, India. The plant was authenticated for its correct botanical identity by the chief botanist.

The aqueous extract of plant was prepared as follows:

400 gms of the chopped, dried flowers of plant were extracted with 2L of distilled water by the soxlet apparatus. The solvent used for obtaining extract was evaporated by a rotator evaporator under reduced pressure at 50 °C. The final extracted material weighed 10 gm that was prepared by dissolving final product in distilled water.<sup>20</sup>

### *Animals*

Swiss albino mice weighing 25-30 grams of either sex were obtained from the central animal house of Narayana Medical College, Nellore. They were housed in standard polypropylene cages with paddy husk as bedding and kept under controlled room temperature (21-23°C; relative humidity 60-70%) in a 12 hours light-dark cycle. Animals were given a standard laboratory diet and water ad libitum. All experiments were performed between 09:00 am and 3:00 pm in order to minimize the effect of circadian rhythms. Animals were acclimatized to laboratory conditions one week prior to initiation of experiments.

### *Method*

#### *The maximal electroshock (MES) induced convulsions*

Albino rats of either sex weighing from 180 to 200 gm were used in this study. These were acclimatized to their environment for one week prior to experimentation. The animals were randomly distributed into four different groups. Each experimental group consists of a 6 animals. Each group is caged separately after recording its body weight and the animals are marked with marker for identification.

### *Equipment*

Electroconvulsimeter (INCO company), ear clip electrodes (150 mA current for 0.2 sec), stop watch.

### *Grouping of animals*

For the experimental animals were weighed, and randomly divided into four groups, each group consisting of six animals.

- Group I - Control group-saline 0.5 ml
- Group II - Standard group- Phenytoin - 25 mg/kg
- Group III - Test group- Rosa damascena - 200 mg/kg
- Group IV - Test group - Rosa damascena - 400 mg/kg.

### *Procedure*

MES seizures were electrically induced by means of an Electroconvulsimeter 150 mA current is delivered transauricularly (ear clips) for 0.2 sec. This current intensity elicited complete tonic hind limb extension (THE) in animals. For measuring various parameters, rats were placed in a clear rectangular plastic cage with an open top, permitting full view of the animals' motor responses to the seizures. Later each animal was then individually observed for 2 hours to study convulsive effects on general behaviour. Suppression of tonic hind limb extension was taken as a measure of efficacy of the drugs in this test. Anti-convulsive drugs abolish or reduce the duration of time of tonic hind limb extension phase of MES. After 30 minutes of administering respective drugs of those particular groups, MES was induced. Onset and duration of time for tonic hind limb extension (THE) was noted and compared the in all groups.

### *Pentylenetetrazole induced seizures*<sup>21</sup>

Albino rats of either sex weighing from 150 to 200 gm used in this study. These were acclimatized to their environment for one week prior to experimentation. The animals were randomly distributed into four different groups. Each experimental group will consist of a 6 animals. Each group is caged separately after recording its body weight, and the animals were marked with marker for identification.

### *Grouping of animals*

The experimental animals were weighed, and randomly divided into four groups, each group consisting of six animals.

- Group I - Control group - saline 0.5 ml
- Group II - standard group- Sodiumvalporate - 200 mg/kg
- Group III - Test group- Rosa damascena - 200 mg/kg
- Group IV - Test group - Rosa damascena - 400 mg/kg.

### Principle

Pentylenetetrazole is a central nervous system stimulant. It produces jerky type of clonic convulsions in rat. The convulsive effect of this drug is considered to be analog to petitmal type of convulsions in man. Pentylenetetrazole has been reported to act through GABA- benzodiazepine receptor mechanisms in the brain. It is widely used as a tool in experimental pharmacology to study convulsant and anticonvulsant action of drugs.

### Procedure

Rats were divided into 4 groups; each group consisted of 6 rats. Rats were chosen by giving pentylenetetrazole. Only those rats which produced jerky movements of the whole body were chosen for the study. After 30 minutes of administering respective drugs of those particular groups, pentylenetetrazole was injected to the animals and the onset and duration time for clonic convulsions are noted in all the groups. Later the onset and duration time for clonic convulsions in all groups was compared.

All the experimental procedures and protocols used in this study were carried out according to the guidelines of institutional animal ethical committee and Ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee).

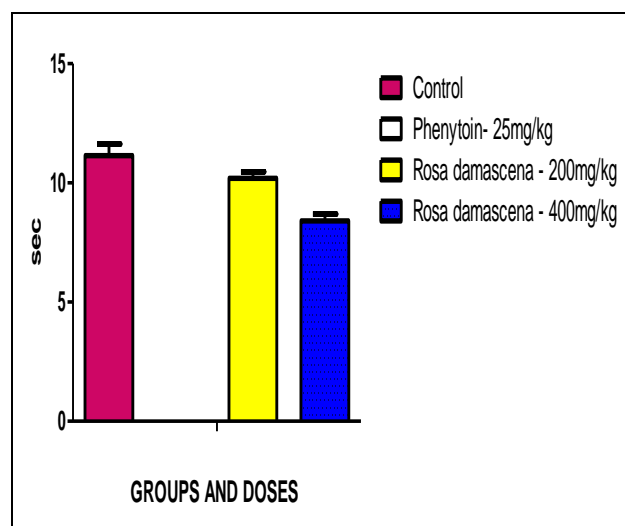
### RESULTS

The time of onset and duration of tonic hind limb extension for control group was  $2.00 \pm 0.196$  and  $11.15 \pm 0.48$  respectively. For *Rosa damascena* the onset and duration of the for dose of 200mg/kg was  $2.50 \pm 0.196$ ,  $10.20 \pm 0.27$  and for 400 mg/kg was  $4.51 \pm 0.20$ ,  $8.41 \pm 0.28$  respectively. The tonic hind extension was totally abolished in standard group. As compared to control group *Rosa damascena* in the dose of 400 mg/kg significantly ( $***p < 0.001$ ) reduced the onset and duration of tonic hind extension, but less when compared to standard group.

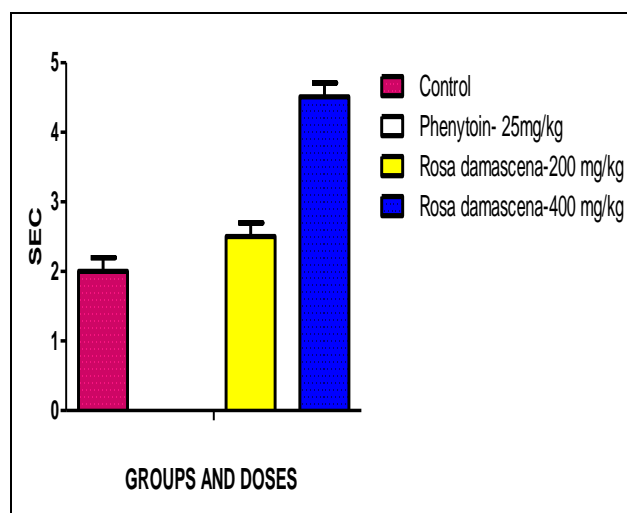
**Table 1: Maximal electroshock seizure (MES) induced convulsions.**

Groups	Treatment groups	Onset of tonic hind limb extension (in sec)	Duration of tonic hind limb extension (in sec)
Control	Normal saline	$2.00 \pm 0.196$	$11.15 \pm 0.48$
Standard (phenytoin)	25 mg/kg	Totally abolished	Totally abolished
<i>Rosa damascena</i>	200 mg/kg	$2.50 \pm 0.196^{***}$	$10.20 \pm 0.27^{***}$
<i>Rosa damascena</i>	400 mg/kg	$4.51 \pm 0.20^{***}$	$8.41 \pm 0.28^{***}$

\*\*\*  $p < 0.001$  compared to control group.



**Figure 1: Mean time for onset of the tonic hind limb extension.**



**Figure 2: Mean time duration of the tonic hind limb extension.**

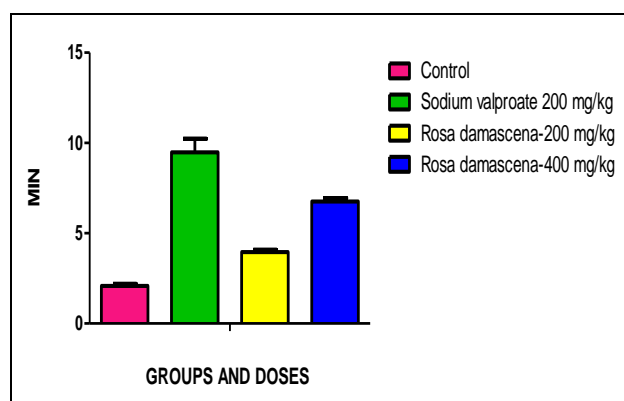
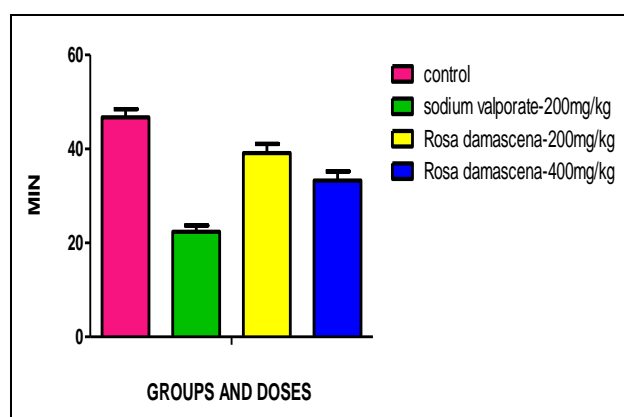
**Table 2: PTZ induced convulsions.**

Groups	Treatment Dose (mg/kg)	Onset of mean time for jerks in minute (SD)	Mean time duration jerks in minute (SD)
Control	Normal saline	2.08±0.12	46.70±1.79
Standard	Sodium valproate - 200 mg/kg	9.48±0.75***	22.36±1.38***
<i>Rosa damascena</i>	200 mg/kg	3.96±0.12***	39.14±1.92***
<i>Rosa damascena</i>	400 mg/kg	6.76±0.18***	33.30±1.90***

\*\*\* p<0.001 compared to control group.

The time of onset of jerks and duration of jerks for control group was 2.08±0.1 and 46.70±1.79. For sodium valproate the onset and duration of jerks was 9.48±0.75 and 22.36±1.38. Onset and duration of jerks for *Rosa damascena* for the dose of 200mg/kg was 3.96±0.12, 39.14±1.92 and for 400 mg/kg is 6.76±0.18, 33.30±1.90 respectively.

As compared with control group *Rosa damascena* significantly (\*\*\*p<0.001) delayed the onset and duration of convulsions induced by PTZ. *Rosa damascena* in the dose of 400 mg/kg significantly delayed the onset of clonic convulsions induced by PTZ, which is comparable with standard drug sodium valproate.

**Figure 3: Mean time for onset of jerky movements.****Figure 4: Mean time duration of jerky movements.**

## DISCUSSION

Pentylentetrazol is a tetrazole derivative with consistent convulsive effect which acts by antagonising the inhibitory GABA ergic neurotransmission. PTZ test is used for screening of drugs effective in petitmal epilepsy.

*Rosa damascena* in the dose of 200 mg/kg and 400 mg/kg showed significant anti-epileptic activity in the seizures induced by pentylentetrazole in a dose dependant manner compared to control group (P<0.001) indicating that it has anti-epileptic property however the antiepileptic activity was less than that of sodium valproate.

*Rosa damascena* increased the seizure threshold, the ability of *Rosa damascena* to both elevate seizure threshold and block PTZ-induced convulsions can be attributed to its modulatory effect on GABA neurotransmission. The probable mechanism of anti-epileptic activity is by increasing the GABA ergic neurotransmission. As GABA is inhibitory neurotransmitter in brain increasing GABA levels suppress the seizure activity in brain.

Our studies is supported by Hosseini M et al showed anticonvulsant activity of *Rosa damascena* in doses of 200 mg/kg in PTZ induced convulsions with respect to activity of Na<sup>+</sup>/K<sup>+</sup>, Mg<sup>2+</sup> and Ca<sup>2+</sup>-ATPases in rat brain during pentylentetrazole-induced epilepsy. All the three ATPases were elevated in different regions of brain during pre-treatment with *Rosa damascena* extracts in PTZ-induced epileptic animal and maintaining ionic equilibrium.<sup>22</sup>

Maximal electric shock induced convulsions is a best suitable test for evaluating anti-epileptic properties of drugs, because it is the best-validated preclinical test that predicts drugs effective against generalized seizures of the tonic-clonic (grand mal) type.

In our study, *Rosa damascena* showed significant anti-epileptic activity with 400 mg/kg compared to control group but has less when compared to that of standard drug phenytoin. At low dose i.e 200 mg/kg, *Rosa damascena* showed antiepileptic property but it was not significant as compared to control.

MES-induced tonic extension can be blocked by drugs that inhibit voltage dependent Na<sup>+</sup> channels, such as phenytoin, carbamazepine, and valproate (Macdonald and Kelly, Rogawski and Porter, White) and drugs that enhance GABA-A receptor-mediated inhibitory neurotransmission, such as benzodiazepines, phenobarbital and valproate (Macdonald and Kelly, Rogawski and Porter, White).

As MES is suppressed by drugs that enhance GABA-A receptor-mediated inhibitory neurotransmission the probable mechanism of *Rosa damascena* to show activity in MES induced convulsion is through GABA-A mediated neurotransmission.

## CONCLUSION

Anticonvulsant property is studied using MES induced convulsions and PTZ induced convulsion in rats. *Rosa damascena* was used in the dose of 200 mg/kg, 400 mg/kg. *Rosa damascena* in the dose of 400 mg/kg showed more significant response than 200 mg/kg by decreasing the time for onset and duration of tonic hind limb extension.

*Rosa damascena* in both doses showed significant reduction in PTZ induced convulsions. The anticonvulsant activity of *Rosa damascena* in the doses of 200 mg/kg and 400 mg/kg is comparable with that of Sodium valproate.

The results showed more activity in PTZ induced convulsion suggesting that it could be very useful drug in absence seizure. The possible mechanism of anticonvulsant property is increase in GABAergic neurotransmission in brain and maintaining of ionic equilibrium in brain by inhibiting Na<sup>+</sup> channels.

Further studies are required to explore its anticonvulsant activity and the probable mechanism of action and to isolate the active principles from them.

## ACKNOWLEDGEMENTS

Authors would like to express my sincere gratitude to my advisor my HOD, DR. B. L. KUDAGI for the continuous support of my related research study, for his patience, motivation, and immense knowledge. His guidance helped me in all the time. I also thank full to my colleagues Dr. Praveen, Dr. Padmavathi, Dr. Sujith who helped me for my research work. I dedicate my research work heartfully to my Parents.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Kaul VK, Singh V, Singh B. Damask rose and marigold: prospective industrial crops. *J Med Aromat Plant Sci.* 2000;22:313-8.
2. Nikbakh TA, Kafi M, Mirmasoudi M, Babalar M. Micropropagation of damask rose (*Rosa damascena* Mill.) cvs Azaran and Ghamsar. *International J of Agriculture and Biology.* 2005;7(4):535-8.
3. Mahmood N, Piacente S, Pizza C, Burke A, Khan AL, Hay AJ. The anti-HIV activity and mechanisms of action of pure com-pounds isolated from *Rosa damascena*. *Biochem Biophys Res Commun.* 1996;229:73-9.
4. Nikbakht A, Kafi M. A study on the relationships between Iranian people and damask rose (*Rosa damascena*) and its therapeutic and healing Properties. *Acta Hort (ISHS).* 2008;790:251-4.
5. Wood G, Bache F. The dispensatory of the United States of America, 4<sup>th</sup> ed. Philadelphia: Griggand Elliot. 1839;8:80-6.
6. Buckle DR, Arch JRS, Boering NE, Foster KA, Taylor JF, Taylor SG, et al. Relaxation effect of potassium channel activators BRL 38227 and pinacidil on guinea-pig and human airway smooth muscle, and blockade of their effects by Glibenclamide and BRL 31660. *Pulm Pharmacol.* 1993;6:77-86.
7. Libster M. Delmar's integrative herb guide for nurses. Delmar Thomson Learning, Albany; 2002:360-370.
8. Zargari A. Medicinal plants. Tehran: Tehran University Press. 1992;1:281-4.
9. Momeni T, Shahrokhi N. Essential oils and their therapeutic actions. Tehran, Iran: Tehran University. Press. 1991;6:101-8.
10. Green M. The Rose. *Aromatic thymes.* 1999;1:11-5.
11. Oka N, Ikegami A, Ohki M, Sakata K, Yagi A, Watanabe N. Citronellyl disaccharide glycoside as an aroma precursor from rose flowers. *Phytochemistry.* 1998;47:1527-9.
12. Knapp H, Straubinger M, Fornari S, Oka N, Watanabe N. (S)-3,7-Dimethyl-5-octene-1,7-diol and related oxygenated monoterpenoids from petals of *Rosa damascena* Mill. *J Agri Food Chem.* 1998;46:1966-70.
13. Shieber A, Mihalev K, Berardini N, Mollov P, Carle R. Flavonol glycosides from distilled petals of *Rosa damascena* Mill. *Z Naturforsch C.* 2005;60:379-84.
14. Kumar N, Singh B, Kaul VK. Flavonoids from *Rosa damascena* Mill. *Nat Prod Commun.* 2006;1:623-6.
15. Delmar's LM. Integrative herb guide for nurses. Delmar thomson learning, Albany. 2002;2:360-70.
16. Mahmood N, Piacente S, Pizza C, Burke A, Khan AL, Hay AJ. The anti-HIV activity and mechanisms of action of pure com-pounds isolated from *Rosa damascena*. *Biochem Biophys Res Commun.* 1996;229:73-9.
17. Kheirabadi M, Moghimi A, Rakhshande H, Rassouli MB . Evaluation of the anticonvulsant activities of

- Rosa damascena on the PTZ induced seizures in wistar rats. *J Biol Sci*. 2008;8:426-30.
18. Ashrafzadeh F, Rakhshandah H, Mahmoudi E. Rosa damascene oil: an adjunctive therapy for pediatric refractory seizer. *Iranian journal of child neurology*. 2007;1:13-7.
  19. Kheirabadi M, Moghimi A, Rakhhande H, Rassouli MB. Evaluvation of the anticonvulsant activities of rosa damascena on PTZ induced seizures in wistar rats. *Journal of biological sciences*. 2008;8(2):426-30.
  20. Dolati K, Rakhshandeh H, Shafei HN. Antidepressant-like effect of aqueous extract from Rosa damascena in mice Avicenna. *Journal Phytomedicine Autum*. 2011;1(2):91-7.
  21. Trescher WH, Lesser RP. The epilepsies. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD. *Neurology in clinical practice*. 5<sup>th</sup> edition. Philadelphia: Elsevier publication. 2008;18:1909-46.
  22. Hosseini M, Rahbardar MG, Sadeghnia HR. Effects of different extracts of Rosa damascena on ptz induced seizures in mice. *Journal of interogative medicine*. 2011;9(10):1118-24.

**Cite this article as:** Tirupathi H, Golla P. Anticonvulsant effect of *Rosa damascena* in pentylenetetrazole and maximal electroshock induced convulsions in albino rats. *Int J Basic Clin Pharmacol* 2016;5:2071-6.