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

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**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.1-3

The major cultivation areas of *Rosa damascena* in Iran are Kashan, Fars and Azerbaijan, among them Kashan is the most famous one.4 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.5,6

North American Indian tribes used a decoction of the root of *Rosa damascena* plant as a cough remedy to ease children’s cough.7 This plant is also used as a gentle laxative8,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.8,9

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 quercitin.10-16 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. 7-10

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. 23

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

Electroconvulsometer (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 Electroconvulsometer 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-convulsives 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.

Pentylentetrazole induced seizures 21

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. Pentylenetetrazol 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.

| Groups          | Treatment groups | Onset of tonic hind limb extension (in sec) | Duration of tonic hind limb extension (in sec) |
|-----------------|------------------|------------------------------------------|-----------------------------------------------|
| Control         | Normal saline    | 2.00±0.196                               | 11.15±0.48                                    |
| Standard (phenytoin) | 25 mg/kg       | Totally abolished                        | Totally abolished                             |
| Rosa damascena  | 200 mg/kg        | 2.50±0.196***                            | 10.20±0.27***                                 |
| Rosa damascena  | 400 mg/kg        | 4.51±0.20***                             | 8.41±0.28***                                  |

***p<0.001 compared to control group.

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±0.196 and 11.15±0.48 respectively. For *Rosa damascena* the onset and duration of the for dose of 200mg/kg was 2.50±0.196, 10.20±0.27 and for 400 mg/kg was 4.51±0.20, 8.41±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.

![Figure 1: Mean time for onset of the tonic hind limb extension.](image1.png)

![Figure 2: Mean time duration of the tonic hind limb extension.](image2.png)
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.

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.

DISCUSSION

Pentylenetetrazol is a tetrozole derivative with consistent convulsive effect which acts by antagonising the inhibitory GABA eric 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 pentylenetetrazole in a dose dependent 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 eric neurotransmission. As GABA is inhibitory neurotransmitter in brain increasing GABA levels supress 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 + /K + , Mg 2+ and Ca 2+ -ATPases in rat brain during pentylenetetrazole-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.

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 + 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 GABANergic neurotransmission in brain and maintaining of ionic equilibrium in brain by inhibiting Na+ channels.

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

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