

# RESEARCH ARTICLE

## ROSA DAMASCENA OIL: AN ADJUNCTIVE THERAPY FOR PEDIATRIC REFRACTORY SEIZURES

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### Abstract:

#### Objective

Several investigations have demonstrated that Rosa damascena has an inhibitory effect on the hypothalamus and on pituitary system reactivity in the rat; it has also been shown that the essential oil of Rosa damascena has significant antiepileptic effects on pentylentetrazole (PTZ) induced seizures in rats. We aimed at assessing the effects of the essential oil of Rosa damascena when used as an adjunct treatment to treat children with refractory seizures

#### Materials and Methods

In this double-blind clinical trial, conducted as a pilot study between April 2004 and March 2005, we administered essential oil of Rosa damascena to sixteen children with refractory epilepsy as an adjunct therapy, and evaluated its effects.

#### Results

16 patients, age range 3-13 years, were enrolled; 56.3% (n= 9) girls and 43.8% (n= 7) boys.

All has been under treatment for 3-6 weeks (baseline phase). They received either the essential oil or placebo for a period of 4 weeks and *in between these periods, they took only their pre-existing antiepileptic drugs for two weeks (washout phase)*.

The mean frequency of seizures in those using essential oil, showed significant decrease as compared to the controls using placebos (p= 0.00).

#### Conclusion

It can be concluded that the essential oil of Rosa Damascena has beneficial antiepileptic effect in children with refractory seizures.

Keywords: Rosa damascena, refractory epilepsy, children, oil.

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### Introduction

Rosa damascena, an erect shrub 1-2 meter in height, has large, colorful flowers. Today Rosa damascena is highly cultivated for its scent (1-2). This plant contains carboxylic acids, terpenes, myrcene and vitamin c (1, 3, 4). The flowers, petals and hips (seed-pots) of Rosa damascena have been used for medical purposes. Rosa damascena has been used for various conditions including menstrual bleeding, digestive disorders and headache (1-2-3). Its anti HIV and antibacterial effect has also been reported (4-5-6). Certain herbal eye drops (Ophthafare) also contain Rosa (7).

## Materials and Methods

This double blind, placebo controlled study was performed in a tertiary referral center between "April 2004 to March 2005". Sixteen patients were enrolled, following signing of informed consent (table 1). Patients were eligible for enrollment if they were 3-13 years old, and had unequivocal seizures that were refractory to current anti-epileptic drugs (AEDs), and had to have intractable epilepsy according to accepted definition (11). Those who had progressive diseases or cardiac, lung, liver or renal diseases were excluded.

In spring 2004, Rosa damascena was collected from Kalat, in the north-east of Iran; a voucher specimen was preserved in the herbarium of the school of pharmacy, Mashhad university of medical sciences (herbarium No: 254-1804-ol). To prepare the oil for each use, 500 gram of the chopped and dried plant with 5000 ml distilled water, was needed to extract 5 ml oil, using the steam distilled apparatus; the plant ingredient concentration in the essential oil was 10 gr % V/V (8-9-10). A 10% concentration of oil with medium chain triglyceride was prepared and the dose prescribed was 5 mg/kg/dose three times per day (1/20 of experimental dose) (8-9-10); placebo was also administered similarly.

When enrolled for the 3-6 weeks (baseline phase) patients received their customary AEDs, and were observed for the types, frequency and duration of their seizures; they were then initially given either oil or placebo as add-on therapy with 5mg/kg/dose three times per day for four weeks (treatment phase) and after a washout period (2 weeks) they received the other, placebo or oil, while they were blinded to the content. Appointments were scheduled weekly during baseline and treatment phases and all seizure-relevant data were recorded at the beginning and end of each phase. Blood samples were taken and examined for complete blood count (CBC) and liver function tests.

Finally, the response to oil or placebo, and any side reactions were assessed. All analyses were done using the SPSS (version 11.5) statistical software package with nonparametric Wilcoxon and Friedman tests and a P value of less than 0.05 was considered significant. it is also necessary to continue or even increase the respiratory care such as upper airway toilet, suction of secretions, chest physiotherapy, non-invasive oxygen therapy and so on (14). All these measures were applied.

## Results

16 patients aged between 3 to 13 years old (mean=8.6±3.6 years old), were recruited in this pilot study; there were 56.3% girls (n=9) and 43.8% boys (n=7). The mean age at seizure onset was 16.7±15.7 months (3 days to 48 months old). In 62.5% (n=10) of them, history of neonatal seizures was positive; eight patients (50%) received 2 AEDs, six (37.5%) 3 AEDs and two of them took 4 AEDs.

More than one type of seizure was experienced by 56.3% (n=9) of patients, the intractable one was taken into account for classification. Complex partial seizures were seen in 43.7% (n=7), complex myoclonic seizures in 37.5% (n=6), myoclonic absence in 6.2% (n=1), and 12.5% (n=2) had the Lennox-Gaustat syndrome. Electro encephalo graphs (EEGs) and computed tomograms of brain were abnormal in 100% and 68.8% respectively; Results showed 18.7% (n=3) were seizure free, 75% (n=12) had over 50% decrease in seizure frequency and no response to oil was seen in 6.2% (n=1) patient. Comparing daily seizure frequency before and after oil, was significant,  $p=0.007$ , whereas before and after placebo, it was  $p=0.2$ . Neither were any significant differences observed between the baseline phases and treatments (oil or placebo) ( $p=0.00$ ).

One patient manifested nausea and poor appetite. All lab tests yielded normal results.

## Discussion

Epilepsy is a chronic disease that often requires lifelong treatment. In compliance with legal and ethical requirements, the efficacy of new antiepileptic drugs are usually evaluated in short trials as add-on therapy in refractory epilepsy (11). In developing countries, economic factors make it necessary to consider drug prices; herbal drugs are normally cheaper and are usually more accepted among the general population. Rosa damascena products are available in the market. Despite searches, we were unable to find any related documented literature on clinical trials about the anticonvulsant effects of Rosa in humans. Previous experimental studies on the effects of purified essential oil showed doses of 500 and 750 mg/kg to have antiepileptic effects on PTZ induced seizure in rats (8-9-10). In this study, we investigated the effects of Rosa oil on refractory epilepsy in children, and found improvement in 18.7% and

reduction in 75% of attacks. These effects are similar to the those of new AEDs; in a study investigating zonisamide as adjunctive treatment for refractory partial seizures, 28.9% had a reduction in frequency (12) and a report on the efficacy of levetiracetam as add-on epilepsy therapy, showed mean reduction in seizure frequency from baseline, per week over the entire treatment period was 30.6%.(13). Another study, researching the efficacy of cloxazolam as add-on therapy in patients with intractable epilepsy, reported 17% became seizure free and 39% had over 50% reduction in frequency (14).

Rosa damascene contains several components such as geraniol, citranellol, farnesol, nerol, eugenol, citral, terpene, and myrcene(1). The compound(s) responsible for the hypnotic or antiepileptic effects of Rosa damascene have not yet been confirmed; however other plants containing compounds such as flavenoids, terpenes and saponins have been found to have hypnotic effects (15). It can therefore be suggested that these compounds may be the ones responsible for hypnotic effect of Rosa damascena.

Flavenoids with anxiolytic and/or antidepressant activity have also been described in regard to many plant species used in folk medicine to depress the Central nervous system (CNS). This effect has been attributed to their affinity for the central benzodiazepine receptor (16). Hence, it can be suggested that the flavenoid component of Rosa damascena contributes in hypnotic effect of this plant through the benzodiazepine receptors.

Geraniol possesses methoxyphenol forms in its structural pathway. Behavioral studies have shown that a number of methoxyphenols and alkylphenols have hypnotic and anticonvulsant properties. It is conceivable that geraniol may be at least partially responsible for the antiepileptic effects of Rosa damascene through the GABA-system. It has also been reported that saponin regulates the effects of sedatives, hypnotic and anticonvulsants (17), and other investigations have found that eugenol has anticonvulsant, analgesic and local anesthetic effects (18-19). These questions need to be addressed in future studies.

### **Conclusion**

On the basis of our observations, it may be concluded that the essential oil of Rosa damascena has anticonvulsant

effects and can improve seizures in children who are resistant to AEDs. Further, more detailed investigations on patients with refractory seizures to confirm these effects and the relevant mechanisms are recommended.

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**Table 1: Basic clinical data of patients**

Number of patients	Sex M̄ male F̄ female	Age (years)	History of neonatal seizure	Type of seizure, Epileptic syndrome	Antiepileptic drugs	Brain CT scan	SGOT, SGPT, Urea, Glucose	EEG (Before and after treatment)
1	F	3	+	Complex myoclonic Epilepsy	PB+SVP	nl*	WNL**	abn***
2	M	7	-	Complex partial seizure	GPN+CBC PRM+NTZ	abn	WNL	abn
3	M	5.5	+	Complex partial seizure	PHT+CBZ	abn	WNL	abn
4	F	6.5	-	Complex partial seizure	SVP+CBZ	abn	WNL	abn
5	M	13	+	Lennox-Gaustat syndrome	CLZ+TPX+ ETHX	nl	WNL	abn
6	F	9.5	+	Complex myoclonic epilepsy	LMG+NTZ+ TPX	nl	WNL	abn
7	M	10	-	Complex myoclonic epilepsy	ETHX+LMG + SVP	nl	WNL	abn
8	M	9.5	+	Complex partial seizure	VGN+TPX+ CBZ	abn	WNL	abn-----
9	F	6.5	-	Complex partial seizure	SVP+CBZ	abn	WNL	abn
10	M	8.5	+	Complex absence	SVP+LMG	abn	WNL	abn
11	F	9	+	Complex partial seizure	SVP+PB	abn	WNL	abn
12	F	12	-	Complex myoclonic epilepsy	LMG+TPX	abn	WNL	abn
13	M	12	-	Complex partial seizure	PHT+PRM	abn	WNL	abn
14	F	8	+	Complex myoclonic epilepsy	PB+SVP+CL Z	abn	WNL	abn
15	F	8.5	+	Lennox-Gaustat syndrome	PB+SVP+NT Z+LMG	abn	WNL	abn
16	F	10.5	+	Complex myoclonic epilepsy	LMG+NTZ+ KEPPRA	abn	WNL	abn

\*nl: normal

\*\*WNL: Within Normal Limit

\*\*\*abn: abnormal

PB: Phenobarbital  
 SVP: Sodium valproate  
 GPN: Gabapentine  
 CBZ: Carbamazepine  
 PRM: Primidon  
 NTZ: Nitrazepam

PHT: Phenytoin  
 CLZ: Clonazepam  
 TPX: Topamax(Topiramate)  
 ETHX: Ethosuximide  
 LMG: lamotrigin  
 Keppra: Levetiracetam