

ORIGINAL ARTICLE

Study of Sedation, Pre-anesthetic and Anti-anxiety Effects of *Malva sylvestris* Extract in Comparison with Diazepam in Rats

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ABSTRACT

Common mallow, with scientific name *Malva sylvestris*, spreads across the world. Common mallow oil's fatty acids compounds were obtained from different parts of Iran with different weather and were tested. The herb contains Malvine, Malvinine and Malvin glycoside. The herb is used for preparing some sedation drugs which are used in neural stresses, anxiety, migraine, asthmatic coughs, as well as local anesthesia in dentistry. Stuart points out that all parts of Common mallow are used in China traditional medicine. Its seed is used as tonic, strengthening, laxative, diuretic, calmative, gastric anti parasite and narcotic. Masson and Teobold said that *Malva Sylvestris* had a great value for tetanus treatment. *Malva sylvestris* is a real calmative for stomachache and digestive disorders as well as beneficial for cancers, ulcers and rheumatic pains. In the present study, 30 Wistar male rats weighting of 200-230 g and about 3 month aged were used for laboratory experiments. Animals were kept in standard condition, at 20-25°C, 70% humidity and light cycle of 12 hours lighting and 12 hours darkness. Standard foods were used in order to feeding by method of Ad-Libitum in during 24 hours feeding. Specific dishes were used for water. The rats were divided in groups consisted of 5 animals and were placed in especial cages. It can be concluded, generally, that based on different studies the extract of *Malva Sylvestris* may affect via effecting on benzodiazepine receptors connected to GABA receptors (considering its flavonoid content). Based on the obtained results by the present study it can be said that according to sedation process the extract dosage of 450 mg/kg BW, among other dosages, has had more significant results and better sedation, pre-anesthetic and anti-anxiety effect in comparison with diazepam ($P < 0.01$).

Key words: sedation, pre-anesthetic, anti-anxiety, diazepam, rats.

Received 09.07.2013 Accepted 12.09.2013

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INTRODUCTION

Nowadays, medical herbs form an important part of traditional medicine in most countries as well as especial and valuable place in new treatment procedures. In the present study has been attempted to introduce the extract as a pre-anesthetic and anti anxiety medicine which is more effective and has fewer side effects in comparison with chemical drugs. Also, the herb is used for disease treatment in traditional medicine [3, 20-21].

Common mallow, with scientific name *Malva Sylvestris*, spreads across the world. *Malva Sylvestris* oil's fatty acids compounds were obtained from different parts of Iran with different weather and were tested. The herb contains Malvine, Malvinine and Malvin glycoside. The herb is used for preparing some sedation drugs which are used in neural stresses, anxiety, migraine, asthmatic coughs, as well as local anesthesia in dentistry. Stuart points out that all parts of hempseed are used in China traditional medicine [2, 4-6]. Its seed is used as tonic, strengthening, laxative, diuretic, calmative, gastric anti parasite and narcotic. Masson and Teobold said that Common mallow had a great value for tetanus treatment. Common mallow is a real calmative for stomachache and digestive disorders as well as beneficial for cancers, ulcers and rheumatic pains [1, 5-19].

Because of existing of effective materials such as Malvine, Malvinine and Malvin glycoside the herb has sedation and calmative effects. Considering the mentioned items and due to existing Malvin glycoside, the herb has sedation and anti-anxiety effects. In this study, the effect of different doses has been evaluated [2, 7-8].

MATERIAL AND METHODS

Understudied animals

In the present study, 30 Wistar male rats of 200 ± 20 g weighting and about 3 month aged were used for laboratory experiments. Animals were kept in standard condition, at 20-25°C, 70% humidity and light cycle of 12 hours lighting and 12 hours darkness. Standard foods were used in order to feeding by method of Ad-Libitum in during 24 hours feeding. Specific dishes were used for water. The rats were divided in groups consisted of 5 animals and were placed in especial cages.

Obtaining extract:

1000 g dried hempseed was powdered in order to obtain extract from stem and leaves. The powder was soaked in methanol and chloroform (70:30) for at least 24 hours; then, the obtained mixture was entered rotary operator system in vacuum pressure for obtaining raw extract. The resulted raw extract was dissolved in the least quantity of hot methanol followed by freezing at -15°C and was filtered immediately for obtaining fatless extract. The fat-removed extract was dissolved in chloromethane, dried by magnesium sulfate and removed solvent by operator rotary system under vacuum in order to water-remove and obtain pure extract.

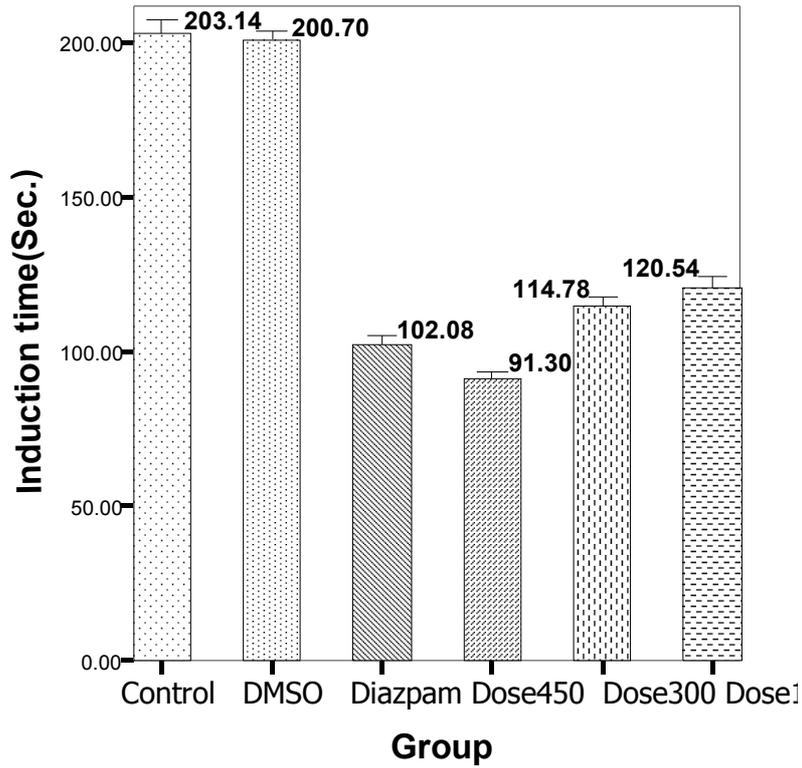
Evaluating method as well as sedation and pre-anesthetic effects of Common mallow:

In order to evaluate the sedation and pre-anesthetic effects of hempseed extract in comparison with diazepam, 150 mg of extract per kg of body weight in first group, 300 mg of extract per kg of body weight in second group, 450 mg of extract per kg of body weight in third group, 1.2 mg diazepam per kg of body weight in fourth group, the same amount of methyl sulfoxide was injected intra peritoneal in fifth group, and sixth group did not receive any drug. 40 mg/kg BW of ketamine was injected intra peritoneal in all groups 30 minutes following of mentioned drugs. Induction time and sleeping time were measured immediately following administration of ketamine.

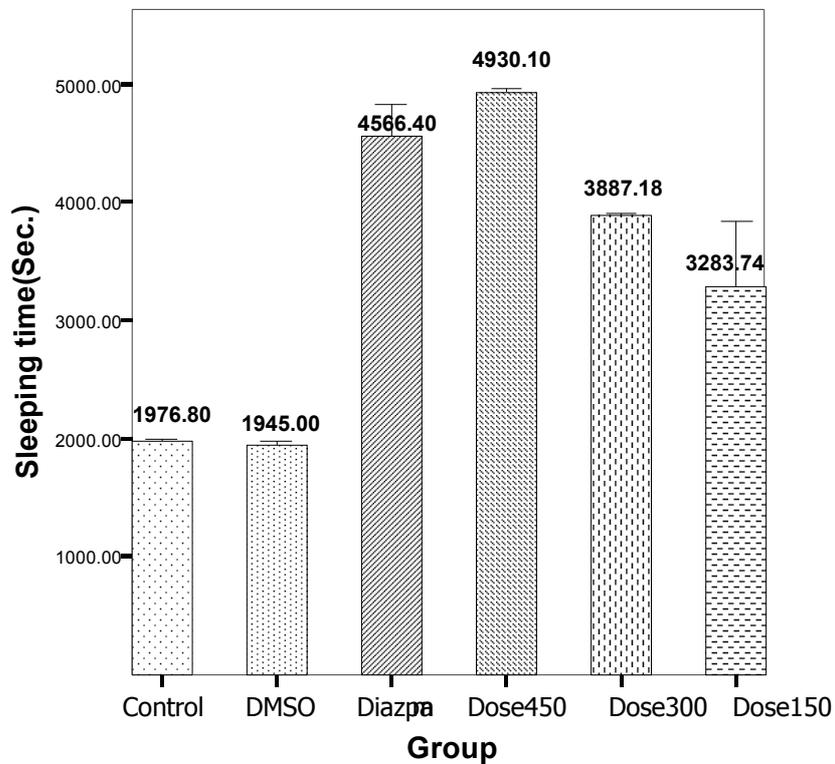
Elevated plus maze was used in order to evaluate anti anxiety effects of Common mallow extract. The system consists of two arms (50×10 cm) which are open and against each other and two arms (40×10×50 cm) which are closed and against each other. They are related to each other by a central plate (10×10 cm) in a semi dark and silent. They are placed in 50 cm distance of the floor. In order to determine anti anxiety effects of the drugs, the duration of remaining the rats on open arms is considered as non-anxiety marker and the duration of remaining the rats on closed arms is considered as anxiety marker. More duration of remaining the rats on open arms demonstrates the strong anti anxiety effects of considered drug. Therefore, Common mallow extract with dosages of 150, 300, 450 mg/kg BW and 1.2 mg/kg BW of diazepam and dimethyl sulfoxide (as placebo) were used as intra peritoneal injection. Methyl sulfoxide was placed in maze center 30 minutes following administration of the mentioned drugs. The time duration in which the rats remained in each of maze's arms was recorded in terms of second; time duration of their presence in maze is 5 minutes [8]. SPSS software program was used in order to statistical analysis of data as well as Tokay follow up test for determining a meaningful difference among dual groups. $P < 0.01$ has been considered as meaningful. Also, data were reported as mean \pm SD.

RESULTS

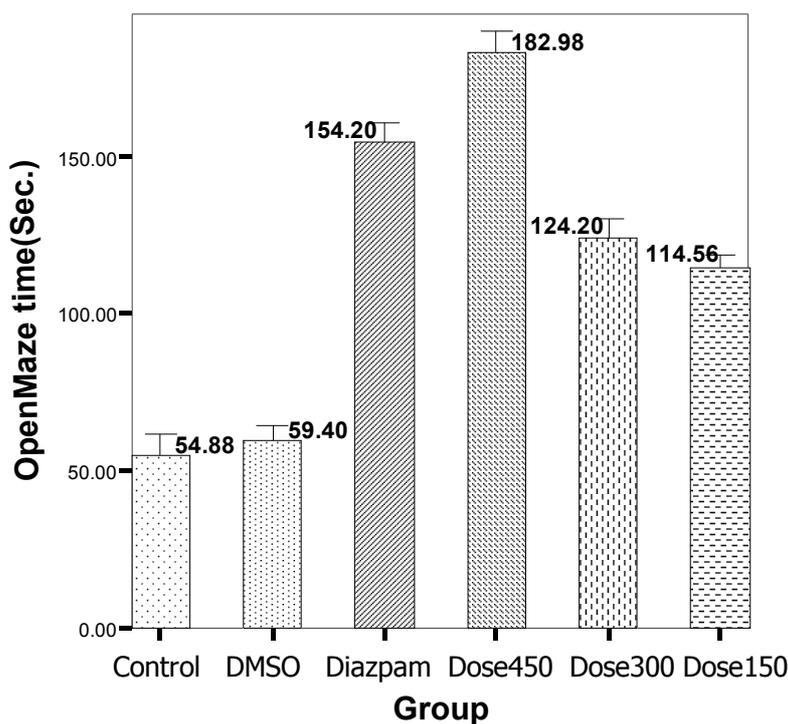
Following the injection of pre-anesthetic drugs and anesthetic inductive drugs, recorded of induction time and sleeping time are considered as markers of the sedation rate effects of a pre anesthetic drug. The results demonstrated that the injection of different dosages of the extract caused to increase sleeping time. The results of dual Tokay follow up test showed a meaningful difference between intra peritoneal injections of 400 mg/kg BW of Common mallow extract and 1.2 mg/kg BW of diazepam. Based on diagrams 1 and 2, intra peritoneal injections of 450 mg/kg BW of Common mallow extract has lower induction time and higher sleeping time in comparison with 1.2 mg/kg BW of diazepam; so that there is a meaningful difference ($P < 0.01$). In other words, the extract has better sedation and pre anesthetic effects in comparison with diazepam. But dosages of 150 and 300 mg/kg BW of the extract don't show a meaningful difference with diazepam. Dosages of 150 and 300 mg/kg BW of the extract have weaker and identical functions, respectively, in comparison with diazepam. The significant differences between of extract dosages of 300 and 450 mg/kg BW suggest that the increase of extract dose leads to increase the sedation and anti anxiety effect. Based on diagram 3, the results show that hempseed extract in dosage of 450 mg/kg BW has a better anti anxiety effect in comparison with 1.2 mg/kg BW of diazepam. Also, they show a statistical significant difference. In other words it causes to decrease the anxiety and increase of the time spent on open maze arms as well as increases the numbers of traverse on open arms. But, the extract dosages of 150 and 300 mg/kg BW demonstrate a significant difference, it means that they have a weak function ($P < 0.01$).



Figures 1: Mean of induction time obtained from understudied groups plant Common mallow



Figures 2: Mean of sleeping time obtained from understudied groups plant Common mallow



Figures 3: Mean of Maze data obtained from understudied groups plant Common mallow

DISCUSSION

In the present study two methods, evaluating the sedation and pre anesthetic effect and evaluating of anti anxiety effects, were used for comparing Common mallow extract in comparison with diazepam. Some other researches were conducted in the past; for example, in 1914 and 1920, Hanzlik and et al. suggested that anti-spasm effect had caused to its administration in angina, asthma, gastric muscular fibers contraction and disorders related to smooth muscles spasms [14, 15-16]. Kafaie & Razavi in 2011 demonstrated in their studies that Common mallow liquid extract had long time effects on spatial memory stabilization in rats; they concluded that high injection dosages of the herb's liquid extract causes to some disorders in memory and learning but it causes to memory strengthening in low or moderate dosages [9, 10-11]. Lev-Ran and et al. in 2011 evaluated the difference and quality of the life and mental health of people who uses hempseed in comparison with who don't use it; they reported that the mental ability is lower in people who don't use Common mallow. Evaluation of the use of Common mallow and disorders of its usage was conducted on last twelve months which are 4.1% and 1.5%, respectively. Hayat Gheybi in 2007 conducted a study on the effect of Esfahan variety of hempseed powder on serum lipid of male rats; they concluded that the Esfahan variety of Common mallow contains much amounts of narcotic compounds such as tetra-hydrocannabinols (THC) which does not modify lipid profile. It seems that longtime use of Esfahan variety of hempseed leads to lipid disorders in blood [17, 18-22].

Based on reported studies, different compounds were identified and isolated from hempseed which were mentioned previously. The presence of alkaloid and flavonoid compounds in the herb cause to increase sleeping time due to injection of anesthetic drug that conforms the present study. Based on observations, it can be said that sedation effect of the extract is related to these compounds [7]. Diazepam, on one hand, is as a benzodiazepine drug has sedation and pre anesthetic effects on central neural system and on the other hand is considered as an anti anxiety drug. So, it causes to some sedation and anti anxiety effects by interaction with GABA receptors presented in brain especially in reticular part of middle brain [12].

Based on obtained results, among administered dosages, 450 mg/kg BW of the extract has a meaningful difference with diazepam during sedation process ($P < 0.01$) and has better sedation and pre anesthetic effects in comparison with Diazepam, in fact it has shorter induction time and longer sleeping time in comparison with diazepam so it can be used as pre anesthetic drug instead of diazepam. But, 450 and 150 mg/ kg BW of the extract don't show meaningful difference over diazepam ($P < 0.01$). Extract dosage of 150 mg/kg BW has a weaker function in comparison with diazepam and the extract dosage of 300 mg/kg BW has an identical function in comparison with diazepam. Based on different study in the present study,

in order to obtain suitable dosages, the extract dosages of 150, 300, 450 mg/kg BW were used. Also, in the second part of the study, based on obtained results, it has demonstrated that 450 mg/kg BW of the herb has better anti anxiety effect in comparison with 1.2 mg/kg BW of diazepam. That is, by administrating 450 mg/kg BW the rats remain more time on maze open arm in comparison with diazepam; also their traverse on open arms is greater which is as an anti-anxiety marker. Considered of the herb's flavonoid and alkaloid compounds and obtained results it can be concluded that hempseed has sedation, pre-anesthetic and anti-anxiety effects [12, 13].

Nowadays, the studies on traditional medicine have been increased. But, Common mallow has remained unknown in spite of traditional uses from its stems and leaves. Consideration and observations about the extract's sedation and anti anxiety effects, are require more studies about identification and extraction of the herb's constituents.

CONCLUSION

It can be concluded, generally, that based on different studies the extract of Common mallow may affect via effecting on benzodiazepine receptors connected to GABA receptors (considering its flavonoid content). Based on the obtained results by the present study it can be said that according to sedation process the extract dosage of 450 mg/kg BW, among other dosages, has had more significant results and has a better sedation, pre-anesthetic and anti-anxiety effect in comparison with diazepam ($P < 0.01$).

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How to cite this article

Ali Rezaei, Mehrdad Pashazadeh, Ali Alizadeh, Jafar Mirzazadeh, Shahla Javanian. Study of Sedation, Pre-anesthetic and Anti-anxiety Effects of *Malva sylvestris* Extract in Comparison with Diazepam in Rats. Bull. Env. Pharmacol. Life Sci., Vol 2 (10) September 2013: 24-28