*Research Article*

# Assessment of antidepressant and anxiolytic activities of aqueous extract of *Daucus carota* Peel

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Received: 13 July 2021 Revised: 20 August 2021 Accepted: 27 August 2021

**Abstract**

**Objective:** Aim of present study was to evaluate antidepressant and anxiolytic activities of *Daucus carota* in albino mice. **Material and Methods:** In present study, aqueous extract of *Daucus carota* peels (AEDC) at doses of 75 mg/kg BW (DCE-A) and 150 mg/kg BW (DCE-B) were evaluated for antidepressant and anxiolytic activities. Albino mice of either sex (25-30g) were used for the study. Toxicity studies of AEDC were performed according to Organisation for Economic Co-operation and Development (OECD) guidelines. **Results and Conclusion:** Imipramine was taken as standard drug in forced swimming test (FST) test where DCE-B showed better reduction in the duration of immobility and increases the number of counts rotation more as compared lower dose DCE-A. In hole board test DCE-B showed about same level of response and potency as standard drug diazepam. In elevated plus maze test, DCE-B found to better in average time spent in open arm, decreasing time in the closed arm and increases number of entries in open arm and decreases the closed arm as compared to DCE-A.

***Keywords:*** Antidepressant activity, Anxiolytic activity, *Daucus carota*, Forced swimming test with activity wheel (FST), Elevated plus maze test (EPM), Hole board test (HBT)

## Introduction

Anxiety and depression (leading in extreme cases to suicide) are two pathologies that are among the top in the list of mental disorders. The menace is reaching one in ten people of the world population regardless of region, class or culture. According to the World Health Organization (WHO), depression will become the most leading cause of diseases worldwide (Coumans et al., 2016). and by 2030 depression is expected to be a major reason for disability worldwide (Smith et al., 2016). Such patients especially resist to treatment, and are one of the major causes for nonfatal health problems among young individuals (Noda et al., 2015; Stonckings et al., 2016; WHO Report, 2016). Recent studies have shown that the treatments cost to the global economy is about one trillion dollars annually (Chisholm et al., 2016).

Conventional antianxiety drugs (specially benzodiazepine drugs) produce several adverse reactions such as drowsiness, dizziness, muscle weakness, constipation, nausea, dry mouth and blurred vision. It is estimated that about 100,000 deaths occur annually due to toxicity from such drugs (Haq et al., 2004). With the similar issue, conventional antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), take several weeks for them to reach efficacy, which can be very dangerous for patients at high risk of suicide (Li et al., 2010).

Complementary and alternative plant-derived medications offer a fertile ground for investigating potential antidepressant & anxiolytic agents. Scientific studies on medicinal plants facilitate their use and increase the therapeutic options at reduced cost in relation to existing treatments in order to improve the quality of life of patients (Yunes et al., 2001; Leitão et al., 2009; Figueredo et al., 2014). On the other hand; medicinal plant therapies have shown effective alternatives for the depression treatment. This has led to significantly progress in the search of plants as alternative for treatment of depression disorders, (Machado et al., 2008; World Health Organization, 2011; Buller et al., 2001; Arya et al., 2012) further, the World Health Organization (WHO) estimates that 80 percent of the world population, presently use herbal medicine for some aspect of primary health care(Davidson-Hunt I. 2000**)**.

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DOI: https://doi.org/10.31024/ajpp.2021.7.3.6

Roots of DC found to be used in the management of diarrhoea, acidity, heartburn and ulcers (Zaini et al., 2012). The plant was reported to possess medicinal values such as antifungal, antibacterial, enzyme protective, hepatoprotective activities (Shoba et al., 2008). It is a remedy for fever, gonorrhoea, anorexia, dysentery, sores, and skin diseases. The plant was reported to possess medicinal values such as antifungal, antibacterial, enzyme protective, hepatoprotective activities. *Daucus carota* was reviewed as remedy for fever, gonorrhoea, anorexia, dysentery, sores and skin diseases and antidepressant potential of its ethanolic extract was reported (Patibandla et al., 2014).

Chemical constituents in DC include polyacetylenes like Falcarinol and falcarindiol, pyrrolidine, β-carotene, and lesser amounts of α-carotene and γ-carotene (Baranska et al., 2005). Carrots represent a good source of carbohydrates (with a clear prevalence of non-reducing sugars), minerals (Ca, P, Fe and Mg), vitamins (thiamine, riboflavin, niacin, folic acid, ascorbic acid and alpha-tocopherol) as well as terpene volatile compounds (terpinolene, terpinen and caryophyllene) and soluble phenols, with a high water content ranging from 86 to 89% (Sharma et al., 2012).

Thus the present study has been undertaken to evaluate the antidepressant and anxiolytic effects of aqueous extract of *Daucus Carota* peel in mice by using forced swimming test with activity wheel (FST), hole board test (HBT) and elevated plus maze test (EPM).

## Materials and methods

### Plant material

The plant material of *Daucus carota* (Carrot) was collected from local distributor in Sagar, Madhya Pradesh. The plant material was identified and authenticated from Department of Botany, Dr. H. S. Gour Central University Sagar, Madhya Pradesh, India. The voucher specimen (Bot./H/03/79/14) in the form of herbarium of the plant was deposited at the Department for future reference.

### Preparation of extract

The completely Shade dried peels of *Daucus Carota* were coarsely powered and weighed accurately 100gm packed in soxhlet apparatus and defatted with petroleum ether (60-80 °C). After defatting, the marc was dried at room temperature and it was filtered and evaporated under reduced pressure up to dryness. Obtained solid extract were stored in well closed container. After petroleum ether extraction, obtained marc was taken in a container and water was added. it was then boiled 100 °C till volume of water become one fourth with continuous shaking every 15-30min, it was then filtered and marc was discarded and filtrate was evaporated then collected the dry product and yield was calculated.

### Preliminary phytochemical screening

The preliminary phytochemical investigations were carried out with the aqueous extract of *Daucus carota* for qualitative identification of phytochemical constituents like alkaloid, flavonoids, steroid & phenols etc. by using standard procedures.

### Animals

Albino mice of either sex weighing between 25-30 gm were used in this study. The animals were acclimatized for 7 days and were housed under standard laboratory conditions of temperature (25±2 °C) and relative humidity (55±5%) with a 12:12 light-dark cycle in polypropylene cages.

All the animals were fed with synthetic standard diet and water was supplied ad libitum under strict hygienic conditions. All the experimental protocols were approved by Institutional Animal Ethical Committee (IAEC) of Sagar Institute of Pharmaceutical Sciences, Sagar. All the animal studies were performed as per the rules and regulations in accordance to the guidelines of CPCSEA with registered number as SIPS/EC/2017/73.

All the animals were fasted 3hrs prior to oral administration of vehicle/standard/test compounds during the experiment. All the experiments were carried out during the light period (9:00 to 17:00 hrs) to avoid circadian rhythms.

### Drugs and chemicals

Standard Drug Imipramine (Sigma Life Sciences, Bangalore) and Diazepam (Sigma Life Sciences, Bangalore) has been used to antidepressant activity.

### Acute oral toxicity studies

Toxicity studies of extract were carried out in albino mice of either sex weighing between 25-30g. Studies were performed according to OECD guideline (OECD Report, 2001) No. 423. Four groups of mice comprising three animals each were treated with 5, 50, 300 and 2000mg/kg of the extract orally, via gastric catheter. The animals were then observed continuously for the first 4hrs for any behavioural changes and for mortality if any at the end of 72hrs. All four doses were found to be safe since no animal died even at the dose of 2000 mg/kg when administered orally and the animals did not showed any gross behavioral changes.

### Experimental design

The animals were divided into four groups of six animals each:

Group I – Control (Vehicle treated group, p.o)

Group II – Standard (Imipramine in Forced swimming test with activity wheel (10.5mg/kg BW) and Diazepam in Hole

board test & Elevated plus maze (4mg/kg BW) i.p.

Group III – Low dose of AEDC (75 mg/kg, i.p.)

Group IV – High dose of AECD (150 mg/kg, i.p.)

**Forced Swimming Test (FST) with activity wheel (Nomura et al., 1982)**

The mice were individually forced to swim for 6 min in glass cylinders (height 37 cm, diameter15.5cm), which contained water to a height of 20 cm (25 °C) from which they cannot escape. A small water-wheel was there in the water tank, animal trying to escape runs the wheel and the number of runs serves as a negative measure of immobility. Male mice were placed individually in the water would start swimming desperately to escape, and as a consequence, the wheel would rotate vigorously that was counted automatically by the system. As depressed, it would discontinue the rotation of the wheel. Each mouse was subjected to a pre-trial for 15 min, and the real trial on the next day for 5 min (recorded). All the animals were fasted for 3 hrs prior to the administration of vehicle/standard/test compounds.

**Hole board test**

The exploratory activity of the QCF-21 in mice following administration was determined using the hole-board test (Wolfman et al., 1994). The apparatus used consisted of a white wooden board (60 × 30 cm) with 16 evenly spaced holes (1 cm diameter x 2 cm depth). Each mouse was placed singly at one corner of the board. Dipping of the head into a hole is a typical behaviour of the mouse indicating a certain degree of curiosity. The number of dips in five minutes was recorded. The test was carried out 30 min after i.p. treatment of QCF-21.

**Elevated plus maze test** (Pellow et al., 1985)

This test has been widely validated to measure anxiety in rodents. In brief, 30 min after the treatment, mice were placed for five minutes on an elevated-plus maze consisting of four arms (25 × 7 cm), two with high, black walls (15 cm high) and two without walls. The maze floor was constructed with plywood. Mice were placed in the intersection between the arms (7 × 7 cm), and the number of entries into, and the time spent in, the open arms were recorded. These two parameters were taken as measures of anxiety related behaviour.

**Statistical Analysis**

Results were presented as Mean ± SEM. The data was subjected for statistical analysis by One way analysis of variance (ANOVA) followed by Dunnett's t test and P<0.05*, 0.01** and 0.001*** were considered as significant, P>0.05 was considered as non-significant (ns) Vs Control group.

**Results**

**Preliminary phytochemical screening**

The aqueous extract of *Daucus carota* L. peel was screened for various chemical tests as per the reported methods and was found to contain Alkaloids, carbohydrates, glycosides, phytosterols, proteins, phenols and resins. (Table 1)

**Acute oral toxicity studies**

Toxicity studies of extract were carried out in according to OECD guideline No. 423 with 5, 50, 300 and 2000mg/kg of the extract administered orally. All four doses were found to be safe and the animals did not showed any gross behavioral changes (Table 2).

**Forced swimming test with activity wheel**

Table 3 and Figure 1, present the results of this test. In forced swimming test with activity wheel test animals were treated with two doses of AEDC viz. DCE-A & DCE-B (75 & 150 mg/kg BW, i.p). Imipramine (10.5 mg/kg BW) was taken as standard drug. DCE-B reduced the immobility (66.25%↓) more than the DCE-A (60%↓). Similar trend was observed in the number of counts rotation of activity wheel where, the DCE-B increases the number of counts rotation (87.5%↑)

**Table 1.** Phytochemical constituents of aqueous extract of Daucus carota (AEDC)

| S. No. | Phytochemical constituents | Test | Ethanolic extract of *Daucus carota* peel |
|---|---|---|---|
| 1 | Alkaloids | Mayer's Test | - |
| | | Dragendroff's Test | + |
| | | Wagner's Test | - |
| 2 | Carbohydrates | Molisch's Test | + |
| | | Fehling's Test | + |
| | | Benedict's Test | - |
| 3 | Glycosides | Modified Borntrager's Test | - |
| | | Legal's Test | + |
| 4 | Phytosterols triterpanoids | Liebermann's Test | + |
| | | Salkowaski Test | + |
| 5 | Protein & Amino acid | Ninhydrine Test | - |
| | | Biuret Test | + |
| 6 | Tannin & Phenols | Ferric chloride Test | + |
| 7 | Resins | | + |

**Table 2.** Acute toxicity study of *Daucus carota*

| S. No. | Dose /kg BW | Number of animals | Onset of toxicity | Sign of toxicity | Total duration of toxicity | Number of animal sacrifice |
|---|---|---|---|---|---|---|
| 1 | 5mg | 3 | None | No sign | 14 Days or 72 hrs | Nil |
| 2 | 50mg | 3 | None | No sign | 14 Days or 72 hrs | Nil |
| 3 | 300mg | 3 | None | No sign | 14 Days or 72 hrs | Nil |
| 4 | 2000mg | 3 | None | No sign | 14 Days or 72 hrs | Nil |

**Table 3.** Forced swimming test with activity wheel.

| S. No. | Treatment | Dose (mg/kg, i.p.) | Duration of Immobility (sec.) | No. of counts rotation (swimming/climbing) |
|---|---|---|---|---|
| 1 | Control | - | 80±1.87 | 16±1.87 |
| 2 | Imipramine | 10.5 | 34±1.60** | 32±2.36* |
| 3 | DCE-A | 75 | 32±1.63** | 24±1.87** |
| 4 | DCE-B | 150 | 27±1.16* | 30±1.87* |

Results were analyzed by one-way ANOVA using Dunnett's multiple comparison test; Significance at $^{**}P < 0.01$, $^{*}P < 0.05$ Non Significance (ns) at $P > 0.05$ Vs control.

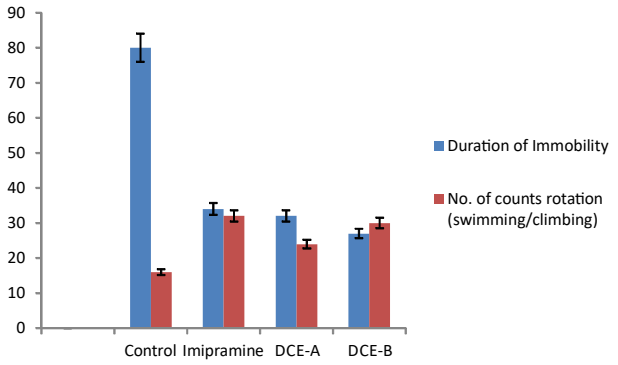


**Figure 1.** Comparative action of DCE-A, DCE-B, control and standard drug in forced swimming test with activity wheel

compared to DCE-A (50.0%↑). Imipramine was found to reduce the duration of immobility (57.5% ↓) and increases the number of counts rotation (100%↑).

## Hole board test

The results are shown in Table 4 and Figure 2. The number of head-dips into the holes of the hole-board apparatus was counted for each animal during a 5-min period. Compared with lipopolysaccharide (LPS), number of head dipping increased (65.2 %↑ ) with diazepam, (63.8 %↑) with DCE-B and (46.37 %↑) with DCE-A.

**Table 4.** Hole board test

| S. No. | Treatment | Dose (mg/kg, i.p.) | No. of head dipping |
|---|---|---|---|
| 1 | Control | - | 14.33±0.01 |
| 2 | Lipopolysacride | 0.8 | 6.90 ±0.02* |
| 3 | Diazepam | 4 | 11.41±0.02** |
| 4 | DCE-A | 75 | 10.1±0.01** |
| 5 | DCE-B | 150 | 11.3±0.02* |

Results were analyzed by one-way ANOVA using Dunnett's multiple comparison test; Significance at $^{**}P < 0.01$, $^{*}P < 0.05$ Non Significance (ns) at $P > 0.05$ Vs control.

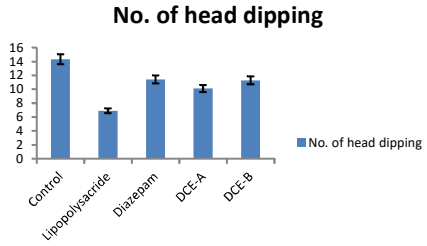


**Figure 2.** Comparative action of DCE-A, DCE-B, control and standard drug in hole board test

## Elevated plus maze test

Results of this test are shown in Table 5, Figure 3 and Figure 4. Standard drugs diazepam at dose 4mg/kg BW increases the average time spent in open arm (~113%↑ ) and decreases the closed arm (36.63%↓) and increases number of entries in open arm (~31.11%↑) and decreases the closed arm (67.10%↓) as compared to control group (p<o.o1). DCE-B (150 mg/kg BW) found to better in average time spent in open arm, decreasing time in the closed arm and increases number of entries in open arm and decreases the closed arm as compared to DCE-A (75 mg/kg BW).

**Table 5.** Elevated plus maze test

| S. No. | Treatment | Dose (mg/kg, i.p.) | Average time spent | | No. of entries | |
|---|---|---|---|---|---|---|
| | | | Open arm | Closed arm | Open arm | Closed arm |
| 1 | Control | - | 1.78±0.06 | 3.33±0.02 | 3.60±0.01 | 7.66±0.03 |
| 2 | Diazepam | 4 | 3.80±0.02* | 2.11±0.34** | 4.72±0.02* | 2.52±0.02** |
| 3 | DCE-A | 75 | 3.22±0.01** | 2.65±0.01** | 4.10±0.38** | 2.94±0.01** |
| 4 | DCE-B | 150 | 3.64±0.01* | 2.50±0.02* | 4.29±0.01** | 2.73±0.02** |

Results were analyzed by one-way ANOVA using Dunnett's multiple comparison test; Significance at $^{**}P < 0.01$, $^{*}P < 0.05$ Non Significance (ns) at $P > 0.05$ Vs control.

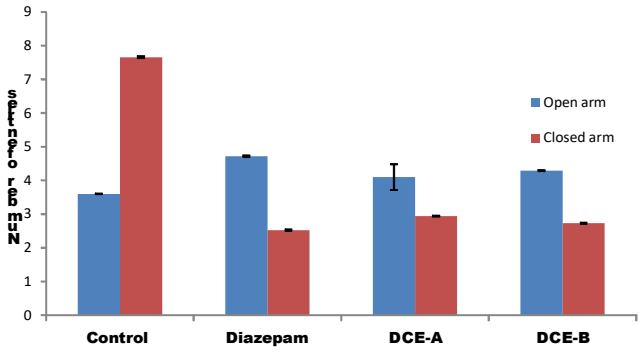


**Figure 3.** Comparative action of DCE-A, DCE-B, control and standard drug in forced swimming test with activity wheel (number of entries in each arm)

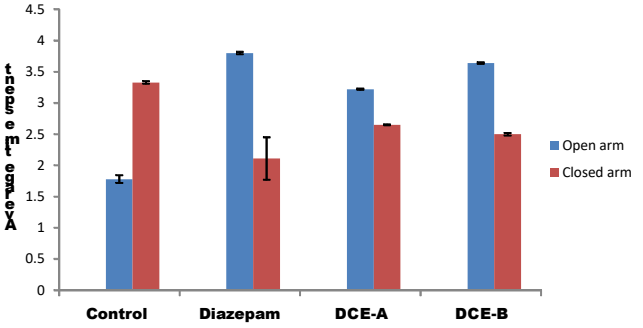


**Figure 4.** Comparative action of DCE-A, DCE-B, control and standard drug in elevated plus maze test (average time spent in each arm)

## Discussion

All the pharmacological evaluation was carried out with 75 and 150 mg/kg BW, i.p, of AEDC. Imipramine was taken as standard drug in forced swimming test with activity wheel while, diazepam was the standard drug in hole board and elevated plus maze tests.

In forced swimming test with activity wheel, it was observed that imipramine (10.5 mg/kg BW) reduced the duration of immobility (57.5% ↓ ) and increases the number of counts rotation (100%↑ ) as compared to control group. DCE-B (75 mg/kg BW) found to reducing the immobility more profoundly than DCE-A (150 mg/kg BW). Similar trend was observed in the number of counts rotation of activity wheel where, the higher dose of extract (DCE-B) found to perform better than the lower dose (DCE-A).

In hole board test, the number of head-dips into the holes of the hole-board apparatus (Ugo Basile, Italy) was counted for each animal during a 5-min period. To avoid disturbing environmental factors, the experimental procedure was carried out in a silent room under dim lights. Compared with lipopolysaccharide (LPS) number of head dipping increased (~65.36 %↑ ) with diazepam (4 mg/kg BW) and DCE-B (150 mg/kg BW) showed about same level of response as standard drug diazepam. DCE-A (75 mg/kg BW) also showed notable head dipping increased.

In elevated plus maze test standard drug diazepam (4mg/kg BW) increases the average time spent in open arm by 113%, decreases the time in closed arm by 36.63%, increases number of entries in open arm by 31.11% and decreases entries in the closed arm by 67.10% as compared to control group with p<o.o1. DCE-B (150 mg/kg BW) found to better in increasing time spent in open arm, decreasing time in the closed arm, increasing number of entries in open arm and decreasing entries in the closed arm as compared to DCE-A (75 mg/kg BW).

## Conclusion

In the present study, AEDC was evaluated for antidepressant activity by using various experimental pharmacological models. Albino mice of either sex (25-30 g) were used for the study. Toxicity studies of AEDC were performed according to OECD guideline No. 423. All four doses (5, 50, 300 and 2000mg/kg p. o.) were found to be safe since no animal was sacrificed and the animals did not show any gross behavioral changes. AEDC at doses of 75 mg/kg BW (DCE-A) and 150 mg/kg BW (DCE-B) were selected for the studies. AEDC at selected doses showed considerable outcomes towards alleviating depressed mood of albino mice in Forced Swim test with activity wheel, hole board test and elevated plus maze test.

In forced swimming test with activity wheel test with imipramine as standard drug higher dose DCE-B showed better reduction in the duration of immobility and increases the number of counts rotation more as compared lower dose DCE-A.

In hole board test DCE-B (150 mg/kg BW) showed about same level of response and potency as standard drug diazepam (4 mg/kg BW). DCE-A (75 mg/kg BW) also showed notable head dipping increased.

In elevated plus maze test, DCE-B (150 mg/kg BW) found to better in average time spent in open arm, decreasing time in the closed arm and increases number of entries in open arm and decreases the closed arm as compared to DCE-A (75 mg/kg BW).

From all the above findings, the present investigation

suggests that the aqueous extract of *Daucus carota* peels may possess antidepressant and anxiolytic activities by certain mechanisms, therefore, lend pharmacological credence to the traditional use of this plant in the treatment. However, an extensive Pharmacological study of this plant is required for complete understanding of these activities of aqueous extract of *Daucus carota*. Further investigation should be carried out to isolate and identify the chemical constituent.

**Acknowledgement**

The authors are grateful to the authorities of Sagar Institute of Pharmaceutical Sciences, Sagar, Madhya Pradesh, India, for providing required facilities.

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