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Effect of Menoveda Akira Tablet against Anxiety; an *In-Vivo* Zebra Fish Model Study



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ABSTRACT

Material and Method- The study was conducted in accordance to the CPCSEA Guidelines (711/PO/Re/S/02/CPCSEA) and reference research paper for the testing of experimental fishes to evaluate the efficacy of Anti-Anxiety Efficacy of Polyherbal formulation- Menoveda Akira Tablets on Zebra fish Model. The test sample was dissolved in the purified water, and four pre specified fixed- doses (1mg/L, 2.5mg/L, 5mg/L and 10mg/L) was orally administered in adult zebra fish (approximately 3 months old) by directly dissolving test sample in to water. The body weight of animals was measured at day0 (before the drug administration) and on day 7 (post study). The rate of mortality and general behavior of the animals were observed continuously for the initial 1, 4, and 24 h after the drug administration and then daily for 7 days. Behavioral parameters were performed by using novel diving tank test and light & dark chamber test. After behavioral analysis, biochemical analysis was examined. **Result-** In present study, it was observed that in zebra fish with treatment, there is a decrease in Lipid peroxidation (LPO), Acetyl cholinesterase (AChEs) and Nitrite level where as increase in levels of Glutathione (GSH). Until seven days after the last dose of the medication was administered, no animal deaths were noticed. For all treatment doses, no abnormalities were seen in any animals until 7 days after the medication was administered. No discernible variation has been found. In the study, weight gain or decrease cannot be interpreted as a symptom of anxiety illness. At doses of 1, 2.5, 5, and 10mg/L, no abnormalities were seen in any zebra fish. **Conclusion-** According to the study's findings, Menoveda Akira Tablets have antioxidant activity, lowers LPO, AChEs & Nitrite Levels, Improves GSH and there was no mortality. Throughout the examination, no abnormalities were seen. So, this product can be used to treat stress- Neuro, Behavioral and Oxidative.



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INTRODUCTION

Anxiety is a psychological and physiological condition that has many different characteristics, including cognitive, emotional, behavioural, and physical. The word "anxiety" is actually derived from the Latin verb "ango," which meaning "to vex or torture," whether or not there is any psychological stress present. Moreover, it may induce feelings of apprehension, fear, and unease. It is sometimes regarded as a typical response to a stressor. A significant mental disease called anxiety causes a variety of functional impairments that have societal implications.

There are 4 types of anxiety:

- Generalized anxiety disorder
- Specific phobias
- Social anxiety
- Panic disorder^[1]

For the treatment of anxiety, a variety of medications, both synthetic and natural, are used. Many synthetic items can irritate the skin and cause rashes and erythema. Herbs such as Citrus paradise, *A. arvensis* L., *C. nepeta* L., *C. monogyna* Jacq., *H. lupulus* L., *L. nobilis* L., *L. angustifolia* Mill., *M. sylvestris* L., *M. chamomilla* L., *M. officinalis* L., *O. basilicum* L., *P. rhoeas* L., *P. somniferum* L., *R. officinalis* L., *T. platyphyllus* Scop., and *V. officinalis* L^[2] as well as synthetic compounds such as Benzodiazepines like Diazepam, Chlordiazepoxide, Alprazolam, Betablockers like Propranolol and H1 Anti- histamine like Hydroxyzine, are used to treat anxiety.^[3]

Up to 33.7% of people will experience an anxiety disorder at some point in their lives, according to large population-based surveys. There is a clear under diagnosis and under treatment of many disorders. According to the study, there has been no change in the prevalence rates of anxiety disorders in recent years. In cross-cultural comparisons, prevalence rates are quite variable. Cultural influences are less likely to be the cause of this heterogeneity than methodological variances. Although they have a long history, anxiety disorders naturally become less common as people age. Multiple mental illnesses as well as other anxiety disorders frequently co-occur with anxiety disorders.^[4]

Menoveda Akira Tablets is investigational product used for the Anxiety to determine the efficacy. The tablet is manufactured by Menoveda life sciences pvt. Ltd, which contain many active ingredients like Mukta Pishti(white pearl) which is widely used in the Hyperacidity, anxiety, fever, burning sensation etc.^[5], Rauwolfia serpentina has anti-stress, anti-aging and life strengthening activities.^[6], Climbing Ayurvedic plant Asparagus racemosus is well-known for its therapeutic effects on a variety of conditions, including hyperlipidemia, hypertension, angina, dysmenorrhea, anxiety disorders, etc.^[7], Withania somnifera is effective for treating a wide range of problems of the central nervous system (CNS), especially epilepsy, stress, and neurodegenerative illnesses like Parkinson's and Alzheimer's disease, among others.^[8], Centella asiatica for cognitive properties as a brain tonic, in the treatment of mental disorders, and as a memory-enhancing agent etc.^[9], Acorus calamus show therapeutic properties in metabolic and neurological disorders, such as anticonvulsant, antidepressant, antihypertensive, anti-inflammatory etc.^[10], Convolvulus prostratus has various pharmacological activity including CNS depression, anxiolytic, tranquillizing, insomnia, antidepressant, antistress, etc.^[11], Nigella sativa used in neurological and psychiatric problems, e.g., the control of pain, Parkinsonism, epilepsy and anxiety, as well as improvement of memory, alertness, elevation of mood and feeling of good health, etc.^[12], Yashtimadhuor Glycyrrhiza glabra have been employed clinically for their anti-inflammatory, antiulcer expectorant, antimicrobial and anxiolytic activities.^[13], Guduchi or Tinospora cordifolia in countering various disorders and usages as anti-oxidant, anti-hyperglycemic, antihyperlipidemic, hepatoprotective, cardiovascular protective, neuroprotective, osteoprotective, radioprotective, anti-anxiety, etc.^[14], Adhatoda vasica, It has a long history of usage for the treatment of many acute and chronic illnesses, and studies have shown that it is particularly effective for bacterial infections, coughs, bronchial infections, reproductive abnormalities, heart diseases, and many other conditions.^[15], Jatamansi used in depression and anxiety related problems.^[16], Quercus infectoria used as multiple biological activities including anti-inflammatory, anti-bacterial, hepato-protective, anti-diabetic, anticancer, gastro-protective, antioxidant, etc. [17]

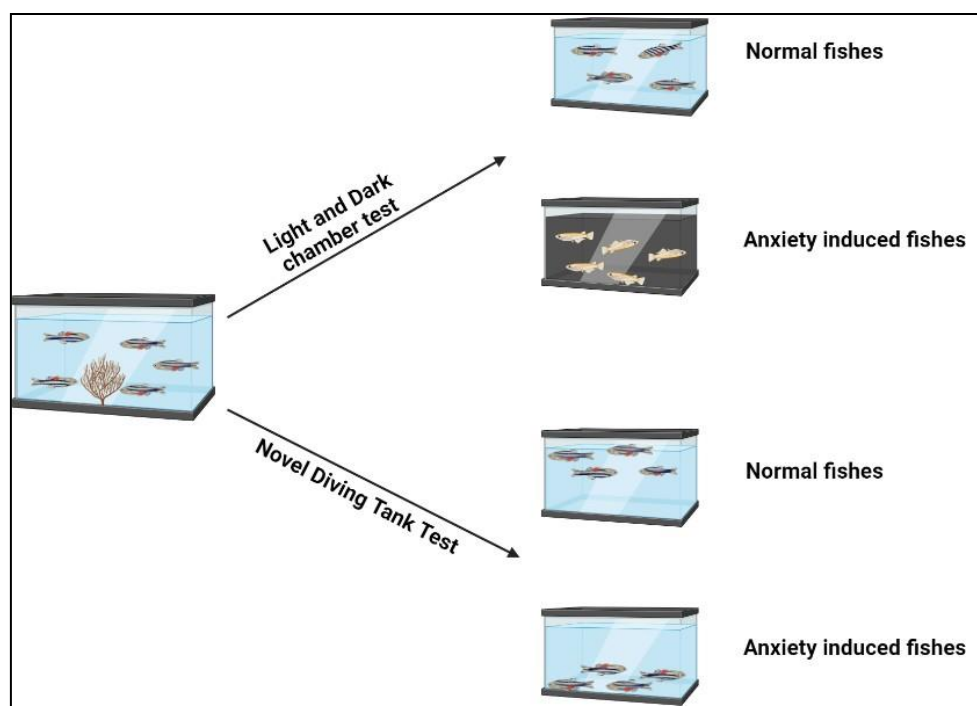


Figure 1: Graphical Abstract of behavioral Analysis using Novel Diving Tank & Light and Darkchamber Test Apparatus

MATERIAL AND METHODS:

The trial was carried out at Department of Pharmacology and Pharmaceutics, Meerut Institute of Engineering and Technology, Meerut. The investigational product called Menoveda Akira Tablets were provided by Menoveda life sciences llp. The Batch Number was MEAK-01, and it was stored at room temperature.

Preparation of Animals:

Adult zebrafish (*Danio rerio*) were randomly selected, weighed, and divided into different groups. A total of seven groups were formed with twelve fishes in each group (Given below). The fishes were kept in the acclimatization period for 14 days prior to dosing in the laboratory conditions maintaining normal room temperature.

Grouping of Animals:

Table 1: AUS–Acute Undetermined Stress

SR.NO.	GROUPS	TREATMENT	NO. OF ANIMALS
1	Normal Control group	Normal	12
2	Negative Control group	Acute unpredictable stress each day for 7 consecutive days.	12
3	Treatment 1 group	Test sample 1mg/L, 24 hours/day. (Orally) against AUS group.	12
4	Treatment 2 group	Test sample 2.5mg/L, 24 hours/day. (Orally) against AUS group.	12
5	Treatment 3 group	Test sample 5mg/L, 24 hours/day. (Orally) against AUS group.	12
6	Treatment 4 group	Test sample 10mg/L, 24 hours/day. (Orally) against AUS group.	12
7	Standard control group	Standard drug (Diazepam) against AUS group (5mg/L; 24 hours/day), (Orally).	12

Preparation of test drug:

Test drug was dissolved in the purified water just prior to the dose administration.

Drug administration:

Four doses 1mg/L, 2.5mg/L, 5 mg/L and 10mg/L for n=6 fishes per liter water were chosen, respectively. Oral route of drug administration was performed.

Mortality observation:

The numbers of animal deaths were observed at day 7, 9, 12, 15, and 17th after drug administration.

General Clinical observation:

Post drug administration, the animals were continuously observed for the behavioral activity (Locomotion, muscle coordination, time spent in specific zone, number of entries) in comparison to zebra fish behavioral models.

Body weight Measurement:

The body weight was measured on day 0 (prior to drug administration) and day 7 (poststudy) using electrical balance.

Biochemical analysis:

At the end of the observation period, the survived animals were sacrificed by cryoanaesthesia and were subjected to biochemical analysis. All biochemical analysis changes were recorded.

Study drug:

Menoveda Akira Tablets is manufactured by Menoveda life sciences Pvt. Ltd, which contains ayurvedic ingredients (Given below):

Table 2: Study drug Ingredients

Sr. No.	Ingredients
1.	Mukta pishti(white pearl)
2.	Rauvolfia serpentina
3.	Asparagus racemosus
4.	Withania somnifera
5.	centella asiatica
6.	Acorus calamus
7.	Convolvulus prostrates
8.	Nigella sativa
9.	Yashtimadhu
10.	Guduchi
11.	Adhatoda vasica
12.	Jatamansi
13.	Quercus infectoria

Study Design-

The study was conducted in accordance to the CPCSEA (711/PO/Re/S/02/CPCSEA) Guidelines and reference research paper for the testing of experimental fishes to evaluate the efficacy of Anti-Anxiety Efficacy of Polyherbal Formulation i.e., Menoveda Akira Tablets on Zebra fish Model.

The test sample was dissolved in the purified water, and four pre specified fixed-doses (1mg/L, 2.5mg/L, 5mg/L and 10mg/L) was orally administered in adult zebra fish (approx. 3 months old) by directly dissolving test sample in to water. The body weight of animals was measured at day 0 (before the drug administration) and on day 7 (post study). The rate of mortality and general behavior of the animals were observed continuously for the initial 1, 4, and 24 h after the drug administration and then daily for 7 days. Behavioral parameters were performed by using novel diving tank test and light & dark chamber test. After behavioral analysis, biochemical analysis was examined.

In the study, no mortality was observed up to 7 days for 1mg/L, 2.5mg/L, 5mg/L and 10mg/L, respectively. No toxic symptoms were found in zebrafish in all four doses. No abnormalities were been observed in general clinical observations or gross necropsy. The normal zebra fish were found to show vigilant behavioral activity with variation in locomotor, behavioral, neurological, or biochemical results when compared to the disease done. No significant changes were observed in the body weight of zebra fish in all four treated doses.

Considering the data obtained from the study, the anti-anxiety drug is effective at the doses of 2.5, 5 and 10mg/L. The drug was found to be in-effective at a dose of 1mg/L.

RESULT AND DISCUSSION

Mortality:

No mortality was observed in any animals until 7 days post drug administration for all the treatment doses.

Clinical signs:

No abnormalities were observed in any animals until 7 days after the drug administration for all the treatment doses.

Body Weight:

No significant variation has been observed. Weight gain or weight loss in the study can not be considered a sign of presence of Anxiety disease.

Macroscopic Findings:

No abnormalities were observed in any zebra fish at 1, 2.5, 5 and 10mg/L dose.

Biochemical analysis:

Test sample possess antioxidant properties. In present study, it was observed that in zebra fish undergone Acute Undetermined Stress (AUS), there is increase in LPO, AChEs and Nitrite levels where as decline in levels of GSH. With zebra fish undergone treatment using test sample, there is decrease in LPO, AChEs and Nitrite levels whereas increase in levels of GSH.

Table: 3 & 4 Behavioral Analysis using Novel Diving Tank Test Apparatus indicating that normal fishes preferring top zone as against the anxiety induced fishes that prefer the Bottom Zone. The fishes were observed for 10 minutes and the observed results are given below:

NOVEL DIVING TANK TEST							
Time spent in TOP ZONE							
Result analysis	Normal control	Negative control	1 mg/L	2.5mg/L	5 mg/L	10 mg/L	Standard control
Behavioral parameters	301 sec.	120.12 sec.	125 sec.	143.10 sec.	167.29 sec.	188 sec.	313.5sec. 10

NOVEL DIVING TANK TEST							
Time spent in BOTTOM ZONE							
Result analysis	Normal control	Negative control	1 mg/L	2.5mg/L	5 mg/L	10 mg/L	Standard control
Behavioral parameters	299 sec.	480.87 sec.	475 sec.	456.89 sec.	432.70 sec.	412 sec.	286.5sec.

Table: 5 & 6 Behavioral Analysis using Light-Dark Chamber Test Apparatus indicating that normal fishes preferring light zone as against the anxiety induced fishes that prefer the dark Zone. The fishes were observed for 10 minutes and the observed results are given below:

LIGHT & DARK CHAMBER TEST							
Time spent in LIGHT CHAMBER							
Result analysis	Normal control	Negative control	1 mg/L	2.5mg/L	5 mg/L	10 mg/L	Standard control
Behavioral parameters	325.75 sec.	55.43 sec.	45.85 sec	152.71sec	189.72 sec	206.66 Sec	287.85 sec.

LIGHT & DARK CHAMBER TEST							
Time spent in DARK CHAMBER							
Result analysis	Normal control	Negative control	1 mg/L	2.5mg/L	5 mg/L	10 mg/L	Standard control
Behavioral parameter	274.25 sec.	544.57 sec.	554.14 sec.	447.28 sec.	410.27 sec.	393.33 sec.	312.14 sec.

CONCLUSION:

In the present research, the work was done on efficacy of Menoveda Akira tablet with the help of various parameters and the behavioral activity was done by using Novel Diving tank test & Light- Dark chamber test.

According to the study's findings, Menoveda Akira Tablets have antioxidant activity, lowers LPO, AChEs& Nitrite Levels, Improves GSH and there was no mortality and abnormalities seen throughout the examination.

So, this product can be used to treat stress conditions such as Neuro, Behavioral and Oxidative.

Declaration of Conflicting Interests: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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