Tianeptine Hemisulfate Monohydrate

Material Lot: 17087102
Country of Origin: China

Analysis

<table>
<thead>
<tr>
<th>Test</th>
<th>Claim</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay</td>
<td>≥98%</td>
<td>99.76%</td>
</tr>
<tr>
<td>Appearance</td>
<td>White crystalline powder, readily soluble in water, dioxane, methanol, EtOH.</td>
<td>Complies</td>
</tr>
<tr>
<td>Solubility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identification</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tianeptine Hemisulfate Monohydrate should be stored at or below room temperature in a tightly sealed durable container. Tianeptine Hemisulfate Monohydrate should be protected from excess heat, direct sunlight, excess humidity and moisture. Tianeptine Hemisulfate Monohydrate has a stable shelf life of 3 years from the date of manufacture when properly stored.

<table>
<thead>
<tr>
<th>Impurity Test</th>
<th>Claim</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss on Drying</td>
<td>≤0.0%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Any single impurity</td>
<td>≤0.2%</td>
<td>0.09%</td>
</tr>
<tr>
<td>Total Impurities</td>
<td>≤0.50%</td>
<td>0.11%</td>
</tr>
<tr>
<td>Residue on Ignition</td>
<td>≤0.1%</td>
<td>0.03%</td>
</tr>
<tr>
<td>Heavy Metal</td>
<td>≤10ppm</td>
<td>Complies</td>
</tr>
<tr>
<td>Assay</td>
<td>99.0-101.0%</td>
<td>99.76%</td>
</tr>
</tbody>
</table>

Precaution and Disclaimer:

This material is sold for research use only. Not for human consumption, nor medical, veterinary, or household uses.

Technical Information:

Application: Improved salt of Tianeptine, used in laboratory research related to major depressive disorder (MDD), also studied for effects on asthma and irritable bowel syndrome (IBS).

Appearance: White powder

Physical State: Solid

Storage / Stability: Tianeptine hemisulfate monohydrate powder is stable for at least four years when stored unopened and calculated at -20 °C.

Modes of Action:

Tianeptine hemisulfate monohydrate is a salt of Tianeptine with potentially improved pharmacokinetic characteristics.

One of the originally hypothesized modes of action for Tianeptine is to increase serotonin (5-HT1) uptake in the brain and in platelets. Unlike most tricyclic compounds, Tianeptine does not appear to be associated with decreases in cognitive performance or motor function (Wagstaff, 2004). More recently, scientific focus has shifted to Tianeptine's activity on the glutamatergic system, particularly including potentiation of the AMPA receptor subtype by activation of CaMKII and PKA via the p38, p42/44 MAPK and JNK pathways, which is hypothesized to represent a novel antidepressant mechanism. By increasing serotonin uptake, Tianeptine has an opposite mechanism to traditional SSRIs. Recent studies have examined the effects of Tianeptine within the framework of the neuroplasticity hypothesis of depression, in which it may have...
some activity. Recent research also shows that Tianeptine may interact with adenine A1 receptors (Elghaw, 2008). [1]

Furthermore, very recent research ... method in 2014 suggests that Tianeptine may act as an α-opioid receptor (MOR) agonist. Researchers used radioligand binding and cell-based functional assays to identify Tianeptine as an effective MOR agonist. It is also a full δ-opioid agonist but at a much lower affinity. Tianeptine was ineffective at κ-opioid receptor sites. The authors suggested activation of MOR or dual activation of MOR and DOR as the initial trigger for Tianeptine's effects (Cagnard, 2014).[3]

Further Scientific research:
Please note that this is an incomplete account of the scientific research on Tianeptine to date. We have made a humble attempt to convey some of the most relevant research on the subject to date, in a variety of applications. However, there is far too much research to condense in this space. For more research, please select a topic and search through the hundreds of journal articles published in PubMed.

Reviews
1. In a review paper published in 2001, researchers found that tianeptine was highly effective in a number of applications. The authors concluded that Tianeptine showed favorable antidepressant activity and was well tolerated throughout previous studies. The researchers recorded an average dosage of around 25 - 50 mg/day. The paper also stated that the biochemical activity of Tianeptine was comparable to a number of classical antidepressants. Common adverse effects include nausea, constipation, gastrointestinal disturbances, headache, dizziness, and dream changes. Hepatotoxicity was rare. (Wager, 2001).[iii]

2. A second review, published in 1999, found similar results. The authors concluded that Tianeptine was an effective antidepressant agent for patients fulfilling the diagnostic criteria of the DSM III for depression. The paper indicated that Tianeptine also had efficacy on anxiety symptoms, the results of which had been confirmed in open long-term trials on elderly people. (Defranney, 1998).[iv]

3. The latest review available on PubMed, published in 2010, indicates that Tianeptine has marked activity in the glutamatergic system. The authors state that these results appear to be consistent with a growing body of research converging on the function of glutamate in neuropsychiatric and depressive. (McEvoy, 2010).[v]

Human studies
1. In a 2015 study, researchers indicated that Tianeptine had no effects on the emotional categorization of cognition. Tianeptine-treated subjects scored lower on facial expression discrimination and had reduced positive affective memory, however, the authors did not state whether or not this was statistically significant (Cayer, 2015).[vi]

2. Three separate double-blind, placebo-controlled studies examined the efficacy of Tianeptine in the treatment of major depressive episodes. The results were published in a 1997 paper. Two of the studies indicated Tianeptine to be an effective antidepressant agent when compared to both placebo and other agents. The third study had an overly high rate of placebo-responders and no conclusion could be made. The author suggested the need for a controlled study to determine the position of Tianeptine among other antidepressants (Cignaroli, 1997).[vii]

3. A third study verified Tianeptine’s action on serotonin uptake. According to the authors, Tianeptine appears to reduce the hypothalamic pituitary adrenal response to stress and to reduce stress-related behavior changes in cerebral morphometry. It may have a neuroprotective effect as an antipsychotic agent and maybe efficacious for post-alcohol-withdrawal symptoms. Significant side effects from Tianeptine include dry mouth, constipation, insomnia, dizziness, and hypotension. However, these side effects appeared to occur more rarely than with other antidepressant agents that were measured (Wilcox, 1995).[viii]

4. In a 2004 study into the effects of Tianeptine on chronic asthma, researchers emphasized the efficacy of Tianeptine in improving these symptoms. Its success was measured over a number of trials, including an open study that lasted for over 7 years and was conducted on over 75,000 asthma patients. The mechanism for this action is hypothesized to be due to its enhancement of serotonin uptake by platelets and serotoninergic axons (Lochm, 2004).[ix]

Toxicity cases
1. At least one case of fatal intoxication with Tianeptine was reported. In 2007, a 26-year-old man was found dead in his bed with a suicide note next to his body. Tianeptine blood concentrations were found: blood 5.1 micro g/ml; urine 2.0 micro g/ml; liver 79 micro g/ml; stomach 73mg. We also had blood alcohol level of 0.83 g/L. The absence of any other suitable causes of death led to the death being ruled as caused by the suicidal ingestion of Tianeptine in combination with alcohol (Poonisa, 2007).[x]

2. One case was reported of a patient who developed hepatitis after taking Tianeptine for 8 weeks. Discontinuing Tianeptine resulted in a complete recovery. The authors suggest that there may be one possibility of hypersensitivity and immuno-allergic mechanisms in hepatotoxicity with Tianeptine (Le Bricqir, 1994).[xi]

Animal studies

“We have moved away from studying human disease in humans ... We all drank the Kool-Aid on that one, me included ... The problem is that it hasn’t worked, and it’s time we stopped dancing around the problem ... We need to refocus and adopt new methodologies for use in humans to understand disease biology in humans,” former NIH Director, Dr. Elias Zerhouni in the June 21, 2013, NIH Record.[xii]

While Newmind values the previous work and research of talented and dedicated scientists on various substances, we also value the principles of ethics towards which many of the world’s top scientists strive. There is already a large amount of data published on Tianeptine’s effects on rodents and small mammals, including toxicity studies on domestic household animals. Please avoid redundancy, especially when it comes to animal research.

1. Research has shown that Tianeptine appears to differ from other antidepressant agents, offering an anxiolytic effect but without similarity to benzodiazepines. In nonhuman animal studies, tianeptine was not found to impair spatial memory. Tianeptine was studied on rats and found to increase compartmental adaptation models in stress. Research data showed that Tianeptine increased the activity of the hippocampus and increased serotonin uptake in rat and human platelets. Data also showed that it decreases OFT and ACTH levels (Kumar, 1989).[xiii]

2. A 1988 study on the neurochemical profile of Tianeptine in nonhuman animals found that it differed significantly from other tricyclic and alternative antidepressant agents. Treatment of rat striatal and rat hippocampal Tianeptine increased serotonin uptake and did not inhibit MAO, MAOA, or MAOB activity. Tianeptine did not bind to any of the following receptors, in vitro: alpha- and beta-adrenergic, dopamine, serotonin, imipramine, GABA, glutamate, benzodiazepine, muscarinic, histamine, Ca2+ channels (Kato, 1988).[xiv]