Studies of Behavioural and Neural Mechanism of Aridanin Isolated from
Tetrapleura tetraptera in Mice

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Abstract: The aim of the present study was to investigate the central nervous system depressant effect and
neural mechanisms of Aridanin in mice. Novelty-induced rearing, head dips, locomotor activity and effect on
learning and memory were studied. Aridanin at 5, 10, 20 and 30 mg kg\(^{-1}\) b.wt. reduced novelty-induced rearing
and locomotor activity in mice. Head dip reduction was noticed only with the highest dose
(30 mg kg\(^{-1}\), i.p.) while in Y-maze, a reduction in number of entrance (locomotion) with no change in percentage
alternation on short term working memory was obtained. Aridanin reversed the central excitatory effect of
flumazenil in the methods. These results confirm the central depressant properties of Aridanin which may be
mediated through GABA\(_{\text{A}}\) receptor.

Key words: Aridanin, Tetrapleura tetraptera, Y-maze, hole board, open field, rearing

INTRODUCTION

Tetrapleura tetraptera Taub (Mimosaceae) locally
known as Aridan is a large tree growing throughout the
rain forest belt of West Africa. It is generally found in the
lowland forest of tropical Africa. The fruit consist of a
fleshy pulp with small, brownish-black seeds. The plant
has many traditional uses mainly in the management of
convulsion, leprosy, inflammation and rheumatic pains,
schistosomiasis, asthma and hypertension (Ojewole and
Adesina, 1983). The dry fruit has a pleasant aroma
(Aladesanmi, 2007). It is used as a popular seasoning
spice, a medicine and a dietary supplement rich in
vitamins in Southern and Eastern Nigeria (Okwu, 2003;
Essien et al., 1994). The fruit is used to prepare soup for
mothers from the first day of birth to prevent post partum
cramp (Nwawu and Akali, 1986). The root extract has
been proven to be useful for the treatment of
gastrointestinal related clinical problem (Noonesi et al.,
1994). The ethanol extract and saponins from the stem
bark of Tetrapleura tetraptera exerted an inhibitory effect
on luteinizing hormone released by pituitary cells,
suggesting its use as contraceptive agent (El-Izzi et al.,
1990). Tetrapleura tetraptera is a natural molluscicide as
aqueous extract of it is effective against Bulimus globosus
and Lymnaea natalensis (Adewunmi, 1991). The
allelopathic potential of Tetrapleura tetraptera has led to
its integration into an agro forestry system (Amoo et al.,
2008). Tetrapleura tetraptera has been shown to improve
the foaming ability of soaps (Adebayo et al., 2000).
Tetrapleura tetraptera has no influence on cell
proliferation and neither induced chromosomal aberration
nor sister chromatid exchanges in Chinese hamster ovary
cells (no genotoxic effect) (Adewunmi et al., 1991).
Tetrapleura tetraptera has been shown to cause
elevation in serum AST and alteration of various
metabolites parameters and did not induce any marked
pathological lesion in the liver (Lawal et al., 2009). The
diuretic, anticonvulsant and analgesic effect of
Aridanin in mice have been reported by Aderibigbe et al.
(2007a, b) and Ojewole (2005). The aqueous extract of
Tetrapleura tetraptera fruit have been shown to
possessed anti-inflammatory and hypoglycaemic
properties (Ojewole and Adewunmi, 2004). The ethanolic
extract of Tetrapleura tetraptera fruit possessed
antiplasmodial activity in mice (Okonkon et al., 2007). One
of the active constituents isolated from *Tetrapleura tetraptera* fruit is a mono-N-acetylglucoside of oleaonic acid (3β-hydroxyolean-12-en-28-oic) called Aridanin (Adesina and Reish, 1985). The present study was carried out in order to investigate further the neurobiology properties of Aridanin.

**MATERIALS AND METHODS**

**Plant material**: Structural elucidation and characterization of Aridanin (Fig. 1) from *Tetrapleura tetraptera* was carried out by Prof. S. K. Adesina, Adesina (Adesina and Reish, 1985) of Drug Research and Product Unit, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife. Sample used for this experiment was collected from him.

**Animals**: Swiss albino male mice weighing between (20-25 g) were obtained in March 2009 from the animal house of the Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife. The animals were divided into five mice in each cage and were fed with a standard laboratory diet and tap water *ad libitum*. The animals were maintained at 25±1°C under natural 12 h day/night conditions. All experiment was carried out in compliance with Obafemi Awolowo University Ethics Committee on research in animals and in accordance with NIH guide for the care and use of laboratory animals.

**Drugs**: Diazepam (Roche, Basel Switzerland), Atropine, Flumazenil, Yohimbine, Naloxone, Cyproheptadine (Sigma Chemicals Co. St. Louis, Missouri, USA).

**Drug dissolution**: Aridanin was dissolved in 5% Tween 80. Diazepam, flumazenil, atropine, yohimbine, naloxone and cyproheptadine were dissolved in normal saline. Tween 80 at 5% concentration did not affect behavioural studies in rodents (Castro et al., 1995). The resulting solution, control vehicle and test materials were usually administered intraperitoneally (i.p.).

**Toxicity**: Acute toxicity studies of Aridanin in mice were carried out as described by Miller and Tainter (1944) and the lethal dose was calculated by the method of Lichtfield and Wilcoxon (1949). It was carried out by injecting Aridanin intraperitoneally (i.p.) into 5 groups of male mice containing 5 animals with the following dose levels 25, 37.5, 50, 75 and 100 mg kg⁻¹. The animals were observed for over 24 h and the LD₅₀ was calculated.

**Novelty-induced rearing**: The behavioural profile of albino mice under the influence of Aridanin was assessed singly in a Plexiglass cage measuring (45 × 25 × 25 cm) containing wood shavings. Behavioural measurements were carried out after i.p. administration of 5% Tween 80 (0.2 mL/20 g) group 1 and Aridanin (5, 10, 20 and 30 mg kg⁻¹, i.p.) groups 2-5. Aridanin was administered for 30 min into animals before been placed singly into an opaque plexiglass observation cage with only one side transparent for observation. Each animal was used only once, with the saw dust bedding changed after each assessment to remove olfactory cue from one animal to the other. The time of the experiment was kept constant (9.00 a.m.-1.00 p.m.) daily to avoid changes in biological rhythm. The behavioural component employed in this observational analysis is rearing. Rearing is defined as the number of times the animal stood on its hind legs or with its forearm against the wall of the observation cage or in the free air (Ajayi and Ukpomnwan, 1994). The frequency of rearing episodes was counted manually for 5 min.

**Locomotor activity**: Motor activity was measured in an open field apparatus consisting of a white plexiglass box (28 × 28 × 25 cm) with a painted back grid dividing the floor into 16 (7 × 7 cm) equal squares. The animals were divided into six groups. Group 1 was given 5% Tween 80 (0.2 mL/20 g i.p.), while groups 2-5 was given Aridanin (5, 10, 20 and 30 mg kg⁻¹ i.p.). Aridanin was administered for 30 min into animals and were placed singly in one of the corners of the box; the number of squares crossed with all four paws was counted for 5 min. The cages were cleared with 70% ethanol at intervals when the animal is removed (Mandal et al., 2001). Diazepam (2.0 mg kg⁻¹, i.p.) group 6 served as reference drug.

**Head dips**: The effect of Aridanin on the rate of head dipping was determined in the holeboard with a number of holes (usually 16) in the floor through which the animal can poke its head. The animals were divided into six groups. Group 1 was given 5% Tween 80
Effect on learning and memory: The Y-maze test can be used as a measure for short term working memory and locomotor activity. Spontaneous alternation is a measure of spatial working memory. To alternate among spatial location, a mouse must remember its previous location. Spontaneous alternation performance was assessed using a Y-maze composed of three equally spaced arms (120°, 41 cm long × 15 cm high). The floors of each arm consist of wood (5 cm wide). This test was carried out using this apparatus to obtain results for spontaneous alternation performance (memory) and locomotor activity (total arm entries). The animals were divided into six groups with (n = 5). Group 1 was given control solution 5% Tween 80 (0.2 mL/20 g, i.p.), while groups 2-5 was given Aradin at the doses of (5, 10, 20 and 30 mg kg⁻¹, i.p.) for 30 min. Each mouse was placed in one of the arm compartments usually arm A for consistency and was allowed to move freely for 5 min without rein forces. An arm entry is defined as the body of a mouse except for its tail completely entering into an arm compartment. The sequence of arm entries is manually recorded. An alternation is defined as an entry into all three arms on consecutive devices. The percentage alternation was expressed as the ratio of actual alternations to possible alternations (defined as the total number of arm entries minus two) multiplied by 100. 70% of ethanl was used to clean the Y-maze at interval (Akanmu et al., 2007). Diazepam (2.0 mg kg⁻¹, i.p.) group 6 was used as reference drug.

Mechanism of action: In another set of experiment, mice were pre-treated i.p. for 15 min with neurotransmitter blockers to evaluate the mode of actions of Aradin on novelty-induced rearing (NIR) behaviour, locomotor activity, head dip and Y-Maze in mice. The following receptor blockers were used; atropine (muscarinic antagonist 0.5 mg kg⁻¹), yohimbine (α-2-adrenergic antagonist, 1.0 mg kg⁻¹), raloxifene (μ-opioid antagonist, 2.0 mg kg⁻¹), flumazenil (GABA antagonist, 2.0 mg kg⁻¹) and cyproheptadine (5-HT antagonist, 0.5 mg kg⁻¹). The doses administered are the doses that have been found not to induce behavioural studies of their own in experimental animals and as such they only block the receptors involved (Ayoka et al., 2006).

Statistical analysis: All behavioural data was analysed by one way ANOVA and Post hoc tests (Student-Newman-Keuls) were carried out to determine the source of a significant mean effect or interaction. Results are expressed as Mean±SEM, p<0.05 is taken as accepted level of significant difference from control. In all these statistical determination, a computer programme the primer of biostatistics (version 3.01) was used (Glantz, 1992).

RESULTS

Results of toxicity testing: The intraperitoneal LD₅₀ of Aradin in mice was calculated to be 60.0 mg kg⁻¹.

Effect of Aradin on novelty-induced rearing, locomotor activity and head dip in mice: Aradin induced a decrease in NIR, locomotor activity and head dips in mice [F (5, 24) = 225.2, p<0.001], [F (5, 24) = 37.3, p<0.001], [F (5, 24) = 54.1, p<0.001] (Table 1).

Effect of Aradin on learning and memory in mice: Aradin (5-30 mg kg⁻¹, i.p.) induced a reduction in total arm entries (locomotion) [F (5, 24) = 68.7, p<0.001] (Table 2). The doses administered gave a percentage alternation that is approximately equal to that of 5% Tween 80 control (Table 2).

Table 1: Effect of Aradin on novelty-induced rearing, locomotor activity and head dip in mice

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Dose (mg/kg)</th>
<th>NIR/5min</th>
<th>LA/5min</th>
<th>HD/5min</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% Tween 80</td>
<td>0.2 mL/20 g</td>
<td>48.4±1.6</td>
<td>130±2.0</td>
<td>39±1.7</td>
</tr>
<tr>
<td>Aradin</td>
<td>5 mg kg⁻¹</td>
<td>22±4.1*</td>
<td>83±4.4*</td>
<td>39±4.9</td>
</tr>
<tr>
<td>Aradin</td>
<td>10 mg kg⁻¹</td>
<td>17±0.7*</td>
<td>78±9.2*</td>
<td>36±4.9</td>
</tr>
<tr>
<td>Aradin</td>
<td>20 mg kg⁻¹</td>
<td>10±0.7*</td>
<td>58±4.0*</td>
<td>35±4.1</td>
</tr>
<tr>
<td>Aradin</td>
<td>30 mg kg⁻¹</td>
<td>6±0.7*</td>
<td>42±6.1*</td>
<td>26±5.5</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2 mg kg⁻¹</td>
<td>7±0.7*</td>
<td>48±3.3*</td>
<td>13±0.1*</td>
</tr>
</tbody>
</table>

Results are expressed as Mean±SEM, (n = 5-7). One way ANOVA revealed that there is significant difference between various treatment groups. NIR: Novelty-Induced Rearing; LA: Locomotor activity; HD: Head dip; % Tween 80: % Tween 80, *indicate significant difference from 5% Tween 80 control, p<0.05

Table 2: Effect of Aradin on learning and memory in mice

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Dose (mg/kg)</th>
<th>No. of entries/5 min</th>
<th>% Alternation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% Tween</td>
<td>800 mL/20 g</td>
<td>23.0±0.7*</td>
<td>60±2.7</td>
</tr>
<tr>
<td>Aradin</td>
<td>5 mg kg⁻¹</td>
<td>11.0±0.7*</td>
<td>60±2.7</td>
</tr>
<tr>
<td>Aradin</td>
<td>10 mg kg⁻¹</td>
<td>10.4±0.5*</td>
<td>65±3.4</td>
</tr>
<tr>
<td>Aradin</td>
<td>20 mg kg⁻¹</td>
<td>10.6±0.5*</td>
<td>60±4.7</td>
</tr>
<tr>
<td>Aradin</td>
<td>30 mg kg⁻¹</td>
<td>8±0.7*</td>
<td>66±2.5</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2 mg kg⁻¹</td>
<td>12±0.7*</td>
<td>41±0.1*</td>
</tr>
</tbody>
</table>

Results are expressed as Mean±SEM, (n = 5-7). One way ANOVA revealed that there is significant difference between various treatment groups. % Tween 80: % Tween 80, *indicate significant difference from 5% Tween 80 control, p<0.05
Table 3: Effect of Aradinan on novelty-induced rearing, locomotor activity and head dip in the presence of antagonists

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Dose</th>
<th>NIR/5 min</th>
<th>LA/5 min</th>
<th>HD/5 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% TW80</td>
<td>0.2 mL/20 g</td>
<td>48.4±1.6</td>
<td>130.2±5.2</td>
<td>39.8±1.7</td>
</tr>
<tr>
<td>Aradinan</td>
<td>10.0 mg kg⁻¹</td>
<td>17.0±0.7</td>
<td>76.8±9.2</td>
<td>38.4±1.9</td>
</tr>
<tr>
<td>ATR</td>
<td>0.5 mg kg⁻¹</td>
<td>47.0±3.2</td>
<td>127.6±2.3</td>
<td>38.1±1.7</td>
</tr>
<tr>
<td>ATR+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>14.8±2.0</td>
<td>55.2±5.1</td>
<td>32.0±0.9</td>
</tr>
<tr>
<td>YOH</td>
<td>1.0 mg kg⁻¹</td>
<td>40.1±1.3</td>
<td>120.0±7.1</td>
<td>32.5±2.2</td>
</tr>
<tr>
<td>YOH+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>6.8±0.6*</td>
<td>50.2±7.0*</td>
<td>32.2±0.9*</td>
</tr>
<tr>
<td>FLU</td>
<td>2.0 mg kg⁻¹</td>
<td>50.6±2.7</td>
<td>160.0±1.3</td>
<td>52.2±3.5*</td>
</tr>
<tr>
<td>FLU+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>5.0±1.3</td>
<td>33.4±1.6</td>
<td>20.6±1.1*</td>
</tr>
<tr>
<td>NAL</td>
<td>2.0 mg kg⁻¹</td>
<td>41.7±1.4</td>
<td>122.4±2.7</td>
<td>51.4±2.4</td>
</tr>
<tr>
<td>NAL+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>2.6±0.4*</td>
<td>13.8±1.3</td>
<td>15.6±1.7*</td>
</tr>
<tr>
<td>CYP</td>
<td>0.5 mg kg⁻¹</td>
<td>40.6±1.4</td>
<td>127.1±4.2</td>
<td>33.1±2.1</td>
</tr>
<tr>
<td>CYP+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>7.0±0.7*</td>
<td>32.4±1.4*</td>
<td>28.6±1.3*</td>
</tr>
</tbody>
</table>

Results are expressed as means±SEM, (n = 5-7). One way ANOVA revealed that there is significant difference between control and treatment groups. NIR: Novelty-induced Rearing, LA: Locomotor activity, HD: Head dip; 5%TW 80: 5% Tween 80; ATR: Atropine; YOH: Yohimbine; FLU: Flumazenil; NAL: Naloxone; CYP: Cyproheptadine; ARI: Aradinan. *Indicate significant difference from 5% Tween 80 control. P<0.05

Table 4: Effect of Aradinan on learning and memory in the presence of antagonists

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Dose</th>
<th>No. of entrance/5 min</th>
<th>% Alteration</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% TW80</td>
<td>0.2 mL/20 g</td>
<td>23.0±0.7</td>
<td>60.9±2.7</td>
</tr>
<tr>
<td>Aradinan</td>
<td>10.0 mg kg⁻¹</td>
<td>10.4±0.5*</td>
<td>65.3±4.7</td>
</tr>
<tr>
<td>ATR</td>
<td>0.5 mg kg⁻¹</td>
<td>24.2±0.8</td>
<td>63.1±3.1</td>
</tr>
<tr>
<td>ATR+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>8.6±1.1*</td>
<td>65.7±3.3</td>
</tr>
<tr>
<td>YOH</td>
<td>1.0 mg kg⁻¹</td>
<td>24.2±1.3</td>
<td>62.0±4.9</td>
</tr>
<tr>
<td>YOH+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>6.2±0.6*</td>
<td>63.4±3.2</td>
</tr>
<tr>
<td>FLU</td>
<td>2.0 mg kg⁻¹</td>
<td>45.2±2.1*</td>
<td>63.4±3.2</td>
</tr>
<tr>
<td>FLU+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>5.2±0.4*</td>
<td>64.4±4.5</td>
</tr>
<tr>
<td>NAL</td>
<td>2.0 mg kg⁻¹</td>
<td>22.7±0.9</td>
<td>61.0±2.7</td>
</tr>
<tr>
<td>NAL+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>6.2±0.6*</td>
<td>65.4±8.7</td>
</tr>
<tr>
<td>CYP</td>
<td>0.5 mg kg⁻¹</td>
<td>21.9±0.7</td>
<td>61.4±2.7</td>
</tr>
<tr>
<td>CYP+ARI</td>
<td>10.0 mg kg⁻¹</td>
<td>5.8±0.4*</td>
<td>64.6±2.7</td>
</tr>
</tbody>
</table>

Results are expressed as means±SEM, (n = 5-7). One way ANOVA revealed that there is significant difference between control and treatment groups. 5%TW 80: 5% Tween 80; ATR: Atropine; YOH: Yohimbine; FLU: Flumazenil; NAL: Naloxone; CYP: Cyproheptadine; ARI: Aradinan. *Indicate significant difference from 5% Tween 80 control. P<0.05

**DISCUSSION**

Aradinan decreased the NIR behaviour in mice at (30 mg kg⁻¹) but with the other doses the decrease is not dose dependent. On exposure to a new environment mice displayed novelty-induced behaviour syndrome consisting of rearing, grooming, scratching and wet dog shakes. In this study, NIR which is a measure of central nervous system excitation (Ajayi and Ukpongwan, 1994; Labella et al., 1979) was used to test the sedative properties of Aradinan. This inhibition of NIR behaviour suggests that Aradinan possesses sedative action. The work is in agreement with some plants that have been shown to possess strong sedative effect such as *Cissus quadrangularis*, *Spondia mombin*, *Ficus thonningii*, *Stechys lavandufolia*, *Nigella sativa* L. and *Cryptolepis sanguinolenta* (Viswanatha Swamy et al., 2006; Musa et al., 2006; Rabbani et al., 2003; Al-Naggar et al., 2003; Ayoka et al., 2006; Anshah et al., 2008).

Aradinan produced a reduction in locomotor activity at (30 mg kg⁻¹) but with the other doses the reduction is not dose dependent. Locomotion is mediated mainly through dopaminergic pathway (Rang et al., 1999) but other neurochemical pathways have been reported to modulate locomotive activities in animals. This reduction in locomotor activity also confirms the central depressive properties of Aradinan. The reduction in locomotor activity is in agreement with plants that have been reported to inhibit locomotor activity such as *Cissus quadrangularis*, *Spondia mombin* and *Ficus thonningii* (Viswanatha Swamy et al., 2006; Musa et al., 2006; Ayoka et al., 2006).

Aradinan at a dose of 5, 10 and 20 mg kg⁻¹ i.p. produced an increase in number of head dips comparable to 5% Tween 80 control; this shows that Aradinan may possess anxiolytic properties. However, 30 mg kg⁻¹ i.p. of Aradinan produced a significant reduction in head dip when compared to 5% Tween 80 control, showing that Aradinan may be anxiogenic. Hence, at higher dose of Aradinan a sedative effect was produced. The effect of Aradinan is similar to benzodiacepine which at low doses has anxiolytic action and at high doses has anxiogenic effect and plants such as *Cissus cornifolia*, *Careya arborea* which has both anxiolytic and anxiogenic properties (Onaivi et al., 1992; Musa et al., 2008; Kumar et al., 2008). The study is also in conformity with a number of scientific reports which indicated that trotenpenoids produced CNS depressant action, since Aradinan is a triterpenoid sapogenin (Chattopadhyay et al., 2003).
In the Y-maze test, Aridanin at (30 mg kg\(^{-1}\)) decrease total arm entries (locomotor activity) in mice, but with the other doses the decrease in total arm entries is not dose dependent. Aridanin at the doses administered do not affect percentage alternation in mice. Memory is a highly complex process that involved several brain structures as well as the role of several neurotransmitters and neuropeptides (Akarrmu et al., 2007; Steckler et al., 1998). Aridanin at doses of (5-30 mg kg\(^{-1}\) i.p.) has no effect on working memory as the percentage alternation produced is different from that of control.

The NIR behaviour response is regulated by multiple neurotransmitter systems; such transmitters include Gamma-Amino-Butyric-Acid (GABA), opioid and dopamine receptors (Waltling, 1998). The administration of atropine, yohimbine, naloxone and cyproheptadine did not reverse the inhibitory effect of Aridanin on NIR, locomotor activity, and Y-Maze, this suggest that muscarinic, adrenergic, opioid and serotonin receptors are not involved in the inhibitory effect of Aridanin on NIR, locomotor activity and Y-Maze. However, yohimbine and naloxone potentiated the inhibitory effect of Aridanin on NIR. However the presence of atropine, yohimbine, naloxone and cyproheptadine potentiated the inhibitory effect of Aridanin on locomotor activity. Flumazenil, a GABA\(_\alpha\) antagonist increased novelty induced rearing, locomotor activity, head dips and Y-Maze which was blocked by Aridanin. This suggests that Aridanin may facilitate GABA\(_\alpha\) transmission (Garrett et al., 2003). The administration of atropine and yohimbine produced a reversal in the reduction of head dip produced by Aridanin. Naloxone potentiated the reduction in head dip produced by Aridanin. Cyproheptadine did not reverse the reduction in head dip produced by Aridanin. The results also show that both cholinergic and adrenergic receptor is partially involved in the exploratory head dip of Aridanin.

The results are in line with previous findings where it was shown that the plant has sedative, anticonvulsant and analgesic effect. Since Aridanin facilitate GABAergic transmission, this may the mechanism of the sedative and anticonvulsant effect of Aridanin.

In conclusion, Aridanin significantly reduced NIR, locomotor activity and head dip in mice. The reduction in NIR, locomotor activity and head dip may be related to an interaction with GABA\(_\alpha\) neurotransmission. This shows that Aridanin may facilitate GABA-ergic neurotransmission. It is known that the inhibitory action of GABA consists of the GABA receptor opening the chloride ion channel to allow more chloride ion to enter the cell, thus making the membrane less likely to polarize (Gottesmann, 2002). It is possible that the sedative effect of Aridanin is mediated by such GABAergic mechanism, since it is known that GABAergic transmission produced profound sedation in mice (Gottesmann, 2002).

REFERENCES


