

# Anxiolytic and CNS Depressant Effects of Aurum Mettalicum by Neuropharmacological Screening

Nusrat Mujtaba<sup>1</sup>, Khan Usmanghani<sup>2</sup>, Subia Jameel<sup>1</sup>, Fatima Qamar<sup>1</sup> and Maria Ayub<sup>1</sup>

<sup>1</sup> Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan

<sup>2</sup> Herbion Pakistan (Pvt.) Limited, Karachi

**Keywords:** Aurum metallicum, Anxiolytic, CNS- depressant

**Author's Contribution**

All the authors contributed significantly to the research that resulted in the submitted manuscripts

**Article info.**

Received: Jan 16, 2018

Accepted: Mar 20, 2018

**Funding Source:** Nil

**Conflict of Interest:** Nil

**Cite this article:** Mujtaba N, Usmanghani K, Jameel S, Qamar F, Ayub M. Anxiolytic and CNS depressant effects of aurum mettalicum by neuropharmacological screening. *RADS J. pharm. pharm. sci.* 2018;6(1):59-66.

**Address of Correspondence**

**Author:**

nusratafzal976@yahoo.com

## ABSTRACT

**Background** The modern available drug therapy is remarkable undoubtedly, but people still convinced to use traditional drugs for different disease condition. In Pakistan, Now a day's homeopathy is accepted worldwide due to its safe therapeutic profile due to minimal adverse reaction associated with homeopathic medicine system.

**Objective:** This study aims to evaluate neuropharmacological effects of Aurum metallicum over psychological behaviors.

**Methodology:** Its anxiolytic activity was checked by head dip, stationary rod and light & dark box. Force swim test showed antidepressants potential of tested drug.

**Result:** Aurum metallicum showed more time spent in light compartment as compare to control demonstrated good anxiolytic activity of Aurum Metallicum. It showed significant anxiolytic activity after 21 days in comparison with control and standard group in head dip cage method. It also showed highly significant antidepressant activity after 21 days dosing in comparison with control in force swim test. Aurum metallicum showed significant increase in grooming behavior, righting reflex, touching sensation, pina and corneal reflex. While salivation, lacrimation, defecation and urination was normal in treated group.

**Conclusion:** The present study concluded that the Aurum metallicum is a gold compound has significant antidepressant activity and anxiolytic activity.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## INTRODUCTION

The modern drug development is remarkable undoubtedly, but people still convinced to use traditional drugs for different disease. Statistically 70% of Population of third-world country rely on alternative-medicine and more comfortable to use these drugs for different chronic ailments. In Pakistan, a large number of population still prefer to use these Complementary and Alternative

Medicines system. A survey was done on complementary and alternative medicine that showed a result of 51.7% of the people in Pakistan uses the CAM- treatment [1].

Samuel Hahnemann about 200 years ago discovered about the complementary and alternative form of medicine that is homeopathy which is based on the law of similar that states

that “let likes be cured by likes”[2]. This mode of treatment is still a choice of treatment as people of this advanced and new era rely on the basis of its dilutions form of medicine with lesser side effects that have a potential to cure a persons in spite of the multiple sayings of the lack of believed persons about homeopathy that it is no more than a placebo remedy[3]. Despite of all sayings, homeopathy is accepted worldwide due to its safety profiles [4, 5]. Most of the people of Pakistan and across the world use homeopathy for different ailments like skin diseases, influenza, headache and gastro-intestinal and musculo-skeletal problems [6-8].

Aurum metallicum commonly called as gold, found in underground soils mainly obtained and exist as a metal [9]. Gold is an element symbolized by Au, comes from Latin derived word Aurum which is used to denote gold. It has 79 atomic-number. Gold remains un-oxidized in air and water hence remains in its original form always. Commercially it is used to manufacture gold coins, art objects and jewelry [10, 11]. Gold is the discrete metal that is generally found in the land-scape in the state of metal, and the first gold compounds that emerge in a steady state are the telluride and stibnite

species, represented as  $AuTe_2$  and  $AuSb_2$  [12,13]. Gold never reacts to sulfuric acid and it is insoluble in nitric acid. Remains un-effected by bases never react with water and basic solutions, however in oxygen presence it may form complexes upon reacting with sodium or potassium cyanide. Metallic gold is mostly diamagnetic in nature [14].

Aurum metallicum is especially used in the treatment of depression which may become as severe to suicidal attempts. Indicated in, unbalanced, self-accusing, negative thinking, suicide, very short tempered, severe pain, hypersensitive to noise, hypercholesterolemia, diabetes, anxiety, ADHD, anemia, post-operative pain Gout, cardiac abnormalities, etc [15]. After 30 years of medical debate, the 1960 report of

the British Empire Rheumatism Council finally confirmed that Aurum metallicum is of significant value in the treatment of rheumatoid arthritis [16]. It was an alchemic medicine between 16th and early 18th centuries. It has also an anti-cancer mechanism [17]. Aurum metallicum used in gram positive infections because it has profound activity against gram positive bacteria like mycoplasma strains and peptic ulcer causing agent *L.H pylori* [18]. The objective of the study was to evaluate the CNS effects of Aurum metallicum after acute dosing.

---

## MATERIALS AND METHOD

---

This study was performed in the research lab of faculty of pharmacy of Jinnah University for women, Karachi from October 2015 to March 2016.

### Material Collection:

Aurum metallicum was procured from homeopathic store Zafar medicine corner located near Nazimabad town Karachi in 3 different potencies of 1M, 200C and 30C packed in a bottle along with dropper. The purchased sample was diluted with small amount of distilled water. No organic solvents were used during whole study. Diazepam and Escitalopram tablets were used as a standard drug for the screening of CNS activity.

### Animal Selection:

Albino mice having weight from 20-26gm bred from the animal house located in department of pharmacology, Jinnah University for Women Karachi were utilized for the screening of CNS parameters. Water, libitum and standard diet of the mice were given properly. The constant environment conditions were maintained as  $23 \pm 2^\circ C$ . The experimental animals were divided into 3 groups. i.e.; Control Group, Treated Group and Standard Group. Regarding the handling of animals, Helsinki Resolution (1964) specifications were followed.

### **Dosing Protocol:**

Aurum metallicum was administered to test animals on regular basis. Dose of Aurum metallicum was adjusted in mg per weight of animals so that every animal received approximately 0.05ml/day (1M strength). Stock solution of 250mg/ml was prepared through serial dilution method in distilled water and administer orally. Diazepam in a dose of 5mg/kg was administered as standard.

### **Experimental protocol:**

Three Groups having 10 animals in each were separated and designated as control group which were received distilled water treated group received Aurum Metallicum in the dose of 0.05ml/day of 1M –strength while standard group received reference drug i.e. Diazepam, 5 mg/kg in screening of antianxiety effects and Escitalopram, 0.5mg/kg in case of antidepressant evaluation. Oral rout was used for administration.

### **CNS Screening Test:**

#### **Light and dark box:**

The light and dark box is made up of wood. Two different chambers of dimensions (25cm×35×35) were used one of them is painted black and further darkened by covering it completely whereas bright chamber is made bright by white painting and illumination with white light of 40W. Both chambers were connected by a small door like way of dimensions (7.5cm×5cm). Every time mice were placed in the center of light box individually after one hour of oral treatment. Ten minutes were taken as cut-off time for experiment. Increase in stay time in the light box is indicative of anxiolytic property of the treated drug [19].

#### **Head dip cage method:**

The Head dip cage method is used to assess emotional reactivity in rodents. Also, called as hole-board test used for the evaluation of anxiety

behaviors. Apparatus comprises enclosed rectangular box (35cm×45cm×45cm) made up of wooden. All of the walls having 2.5cm in diameter holes [68]. Ignorant mice were placed within central region and allow freely exploration for 5 minutes. Readings for mouse stuck out from its snout was recorded. As many as mouse stuck-out snout, it indicates its depression [20].

#### **Stationary rod test:**

Stationary rod test provides a good opportunity to assess, general locomotor activity, and provide a way to analyze anxiety-related behavior in rodents. It has stainless steel rods with two platforms in both ends. Before start of the experiment mice were given a brief training. Before administration of drug albino mice control and treated groups were placed in the center of the rod and allowed to walk separately one by one. The time to reach on other platform was recorded. Observation was recorded for 5 minutes [21].

#### **Forced swim test:**

It is used to evaluate the anti- depressive action of Aurum metallicum. The apparatus FST consists of a cylindrical container made up of glass having 8cm water of temperature ranges 22-25° C [22]. Mice were placed in a glass cylindrical having plenty of water after 30 minutes of administration of drug. Mice was calm and were kept in a cylinder full of water from which mice can't discharge and forced to bath. When mice show the floating posture, the observations were recorded till the fixed posture of mice. Cut-off time was 5 minutes [23]

#### **Gross behavior test:**

Mice were everyday experiential for the gross performance activities counting depression, nervousness, behavior, reactions etc. before and later drug administration. Sedation, mentoring, defecation and escapee actions was sensible in mice Functional Observation Battery: Provides a quantitative behavioral and pragmatic profile by

observational evaluation of mice in thousand and one behavioral and physiological domains, including activity/arousal, generator and autonomic measures, sensory trade and reflexes, neuropsychiatric field, and exhaustive appearance and behaviors[24].

#### Statistical Analysis:

All results were analyzed by SPSS (Statistical Package for Social Sciences). Overall data presented as mean  $\pm$  SD and analyzed following one way ANOVA followed by Tuckey's & Sheffie test by post-hoc analysis.  $p \leq 0.05$  were considered as significant, while  $p \leq 0.005$  considered as highly significant.

## RESULTS AND DISCUSSION

Now a days, homeopathic treatment is introduced conventionally as key part of alternative and complimentary medication-system (CAM) and increasing its popularity day by day among peoples. Conventional available pharmacological treatment is very costly and associated very numerous undesired effects resulting in loss of patient compliance. While homeopathic therapy is very cheap and cost effective [25].

Aurum metallicum is well known homeopathic medicine for the treatment of enhancing motivational activities, as an antidepressant, to cure major depressive disorders, to relief vascular palpitations and insomnia. Aurum metallicum is indicated for wandering the pain in joints and muscles [26].

Anxiolytic activity of the most drugs are mediated by GABA [103].The purposed mechanism for anxiolytic activity of Aurum metallicum might be due to its binding with GABA mediated receptor like benzodiazepine. It can be estimated by the transition numbers between light/dark model compartment and the time consumed in the white box [27].

Table 1 showed the anxiolytic activity of Aurum metallicum in mice after 7days, 14 days and 21 days of dosing in mice by light & dark box apparatus. On day 7 and day 14, after introduction of mice in light & dark compartment Aurum metallicum showed more time spent in light compartment as compare to control but lesser than standard which ultimately demonstrated good anxiolytic activity of Aurum Metallicum.

**Table 1:** Anxiolytic effects of *aurum metallicum* by light & dark box

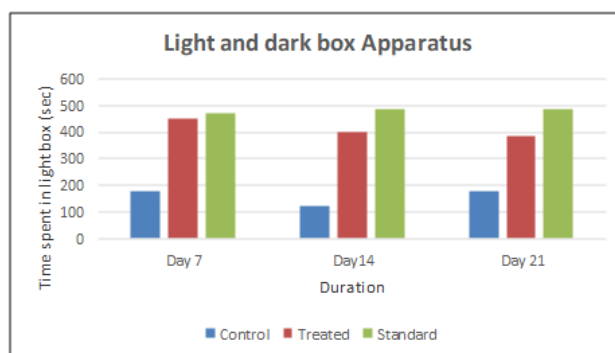
Time spent in light compartment (sec)			
	Day 7	Day 14	Day 21
Groups	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Control	175.8 $\pm$ 3.33	124 $\pm$ 3.4	175.8 $\pm$ 3.48
Treated	448.5 $\pm$ 1.08 <sup>aa</sup>	402.4 $\pm$ 1.9 <sup>aa</sup>	386.5 $\pm$ 1.35 <sup>aa</sup>
Standard	473.2 $\pm$ 2.62	487 $\pm$ 1.49	485.1 $\pm$ 1.45

n= 10

Values are expressed as mean  $\pm$  S.D.

<sup>a</sup> $P \leq 0.05$  as significant, <sup>aa</sup> $P \leq 0.005$  as highly significant compared with control

<sup>b</sup> $P \leq 0.05$  as significant, <sup>bb</sup> $P \leq 0.005$  as highly significant compared with standard



**Figure 1:** Anxiolytic Effects of *Aurum metallicum* by Light & Dark box

n= 10

Values are expressed as mean  $\pm$  S.D.

<sup>a</sup> $P \leq 0.05$  as significant, <sup>aa</sup> $P \leq 0.005$  as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard

Table 2 showed Anxiolytic activity of Aurum metallicum was evaluated by introducing mice into head dip cage apparatus and the test results were evaluated after 7 days, 14 days and 21 days of dosing interval. 3 groups were assessed i.e. Control Group, Treated Group and Standard Group. Aurum metallicum showed significant anxiolytic activity after 21 days in comparison with control and standard group in head dip cage method.

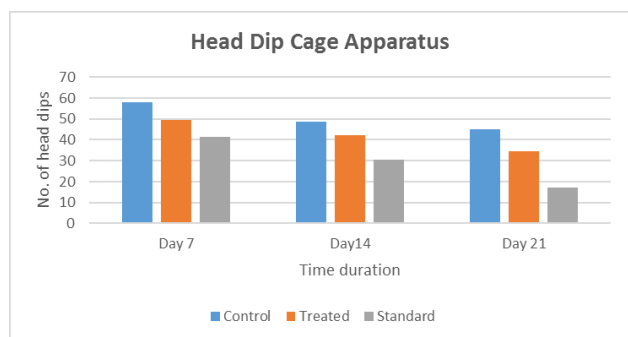
**Table 2:** Anxiolytic Effects of Aurum metallicum by Head dip cage apparatus

Groups	Number of Head Dips (n)		
	Day 7	Day14	Day 21
	Mean± S.D	Mean± S.D	Mean± S.D
Control	58.17 ± 8.13	48.5± 6.68	45.17± 8.13
Treated	49.5± 2.81 <sup>a,b</sup>	42.17 ± 4.87	34.67± 1.21 <sup>a</sup>
Standard	41.5± 9.3 <sup>a</sup>	30.50 ± 14.8	17.33 ±4.36 <sup>aa</sup>

n= 10 Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard



**Figure 2:** Effects of Aurum metallicum by head dip cage apparatus

n= 10 Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard

Table 3 reveals the anxiolytic effects of Aurum metallicum. It showed anxiolytic activity at day 7, 14 and 21 days, some lesser than standard but significantly higher than control.

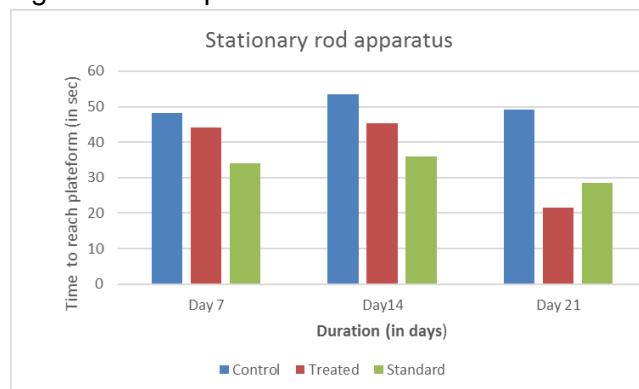
**Table 3:** Effects of aurum metallicum by stationary rod apparatus

Groups	Time to reach the platform (in seconds)		
	Day 7	Day14	Day 21
	Mean± S.D	Mean± S.D	Mean± S.D
Control	48.3 ± 4.7	53.50 ± 5.24	49.17 ± 3.3
Treated	44.17 ± 6.58	45.33 ± 8.91 <sup>a</sup>	21.5 ± 10.8 <sup>aa, b</sup>
Standard	34.0 ± 12.18 <sup>a</sup>	36.0 ± 8.17 <sup>aa</sup>	28.61 ± 12.3 <sup>aa</sup>

n= 10 Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard



**Figure 3:** Effects of Aurum metallicum by stationary Rod Apparatus

n= 10 Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard

Table 4 showed the antidepressant activity of control, Aurum metallicum and Escitalopram 0.5mg/kg as standard on force swim test after 7 days, 14 days and 21 days of dosing. Aurum metallicum showed highly significant antidepressant activity after 21 days dosing in comparison with control.

**Table 4:** Antidepressant *Aurum mettalicum* activity by Force Swim Method

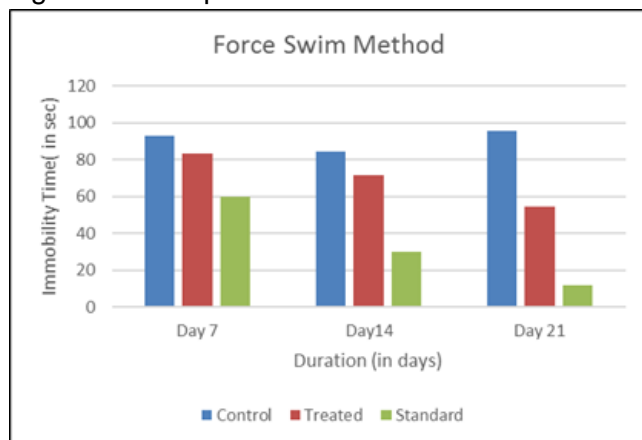
Groups	Immobility Time (in seconds)		
	Day 7	Day14	Day 21
	Mean±S.D	Mean±S.D	Mean±S.D
Control	92.7 ±2.00	84.6± 1.02	95.8 ± 1.02
Treated	83.25 ±1.55 <sup>b</sup>	71.5± 1.55 <sup>b</sup>	54.6 ± 1.08 <sup>aa</sup>
Standard	59.99 ±1.55 <sup>b</sup>	30.00± 1.47	12.01 ± 1.5 <sup>aa</sup>

n= 10

Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard



**Figure 4:** Effects of Aurum metallicum by Force Swim Method

n=8 Values are expressed as mean ± S.D.

<sup>a</sup>P≤0.05 as significant, <sup>aa</sup>P≤0.005 as highly significant compared with control

<sup>b</sup>P≤0.05 as significant, <sup>bb</sup>P≤0.005 as highly significant compared with standard

Table 5 showed effects of different treatment on gross behavioral parameters. Aurum metallicum showed significant increase in grooming behavior, righting reflex, touching sensation, pina and corneal reflex. While salivation, lacrimation, defecation and urination was normal in treated group.

**Table 5:** Assessment of Gross behavioral activities

Parameters	Control	Treated	Standard
Spontaneous Motor Activity	+	+	+
Restlessness	-	-	-
Grooming Behavior	+	++	+
Staggering	-	-	-
Straub's Tail Phenomenon	-	-	-
Writhing Reflex	-	-	-
Tremors	-	-	-
Twitches	-	-	-
Opisthotonic	-	-	-
Escape After Touch	+	+++	++
Righting Reflex	++	++	+
Pina Reflex	+	+	+
Corneal Reflex	+	+	+
Pain Flowing Stimulation	+	+	+
Pupillary Diameter	-	-	-
Ptosis	-	-	-
Exophthalmos	-	-	-
Sweating/ Salivation	Normal	Normal	Normal
Defecation/Urination	Normal	Normal	Normal
Lacrimation	Normal	Normal	Normal
Piloerection	+	+	+
Ataxia	-	-	-
Nystagmus	-	-	-
Passivity	-	-	-

+ ve = represents presence of symptoms

- ve = represents absence of symptoms

---

## CONCLUSION

---

From above study, we can conclude that Aurum metallicum has significant antianxiety and antidepressant effects. Its anxiolytic activity was checked by head dip, stationary rod and light & dark box which showed its significant anxiolytic and memory enhancing activity. Force swim test also showed significant antidepressant activity after continued dosing. Further studies are suggested to illustration for activities of Aurum metallicum.

---

## REFERENCES

---

1. Khan HH, Niazi AK, Ghazanfar H, Khan GH, Chaudhry MA, Khan ZH, Assad S, Khan LH, Oureshi MO, Orakzai SH. Use of complementary and alternative medicine in orthopedic patients in Pakistan: A cross-sectional study. *Rawal Medical Journal*. 2015;40(3):294-8.
2. Shah SF, Mubeen SM, Mansoor S. Concepts of homeopathy among general population in Karachi, Pakistan. *JPMA*. 2010;60(667).
3. Shah SF, Mubeen SM, Mansoor S. Concepts of homeopathy among general population in Karachi, Pakistan. *JPMA*. 2010;60(667).
4. Dantas F, Rampes H. Do homeopathic medicines provoke adverse effects? A systematic review. *British Homoeopathic Journal*. 2000;89:S35-8.
5. Avello ML, Avendaño CO, Mennickent SC. General aspects of homeopathy. *Revista medica de Chile*. 2009 Jan;137(1):115-20.
6. Malik IA, Khan NA, Khan W. Use of unconventional methods of therapy by cancer patients in Pakistan. *European Journal of Epidemiology*. 2000; 16(2):155- 60.
7. Qidwai W. Utilization of services of Homeopathic Practitioners among patients in Karachi, Pakistan. *Headache*. 2003; 8:12.
8. Sevar R. Audit of outcome in 455 consecutive patients treated with homeopathic medicines. *Homeopathy*. 2005; 94(4):215-21.
9. Jain A. Does homeopathy reduce the cost of conventional drug prescribing? : A study of comparative prescribing costs.
10. Crawley J, Goodwin FK. Preliminary report of a simple animal behavior model for the anxiolytic effects of benzodiazepines. *Pharmacology Biochemistry and Behavior*. 1980; 13(2):167-70.
11. Bellavite P. Complexity science and homeopathy: a synthetic overview. *Homeopathy*. 2003; 92(4):203-12.
12. Rutten A, Stolper C. The 2005 meta-analysis of homeopathy: the importance of post-publication data. *Homeopathy*. 2008; 97(4):169-77.
13. Assié M-B, Chopin P, Stenger A, Palmier C, Briley M. Neuropharmacology of a new potential anxiolytic compound, F 2692, 1-(3'-trifluoromethyl phenyl) 1, 4-dihydro 3-amino 4-oxo 6-methyl pyridazine. *Psychopharmacology*. 1993; 110(1-2):13-8.
14. Sandra E. Chronic diazepam treatment: effect of dose on development of tolerance and incidence of withdrawal in an animal test of anxiety. *Human Psychopharmacology: Clinical and Experimental*. 1989; 4(1):59-63.
15. Kryachko ES. Interaction of Gold Atom with Clusters of Water: Few Computational Mise-En-Scènes with Hydrogen Bonding Motif. *Collection of Czechoslovak Chemical Communications*. 2008; 73(11):1457-74.
16. Keppler BK. *Metal complexes in cancer chemotherapy: wiley-VCH*; 1993.
17. c.x Mirabelli RKJ, S.T. Crooke, M.R. Mattern, S.M. Mong, e.M. Sung, G. Rush, S.J. Berners-Price, P.S. Jarrett and P.J. Sadler, in '5th International Symposium on Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy', ed. M. Nicolini and G. Bandoli, Cleup, Padua, Italy, 1987, p. 319.
18. Pricker SP. Medical uses of gold compounds: past, present and future. *Gold bulletin*. 1996; 29(2):53-60.
19. Dias f, takahashi c. Cytogenetic evaluation of the effect of aqueous extracts of the medicinal-plants alpinia-nutans rosc (zingiberaceae) and pogostemun-heyneanus benth (labiatae) on wistar rats and allium-cepa linn (liliaceae) root-tip cells. *Revista brasileira de genetica*. 1994; 17(2):175-80.
20. Thippeswamy B, Mishra B, Veerapur V, Gupta G. Anxiolytic activity of *Nymphaea alba* Linn. in mice as experimental models of anxiety. *Indian journal of pharmacology*. 2011; 43(1):50.
21. Kishioka A, Fukushima F, Ito T, Kataoka H, Mori H, Ikeda T, et al. A novel form of memory for auditory fear conditioning at a low-intensity unconditioned stimulus. *PLoS One*. 2009; 4(1):e4157.
22. Crawley JN. *What's wrong with my mouse? : Behavioral phenotyping of transgenic and knockout mice: John Wiley & Sons*; 2007.
23. Santarelli L, Saxe M, Gross C, Surget A, Battaglia F, Dulawa S, et al. Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. *Science*. 2003; 301(5634):805-9.
24. Yam VW-W, Cheng EC-C. Highlights on the recent advances in gold chemistry—A photophysical perspective. *Chemical Society Reviews*. 2008; 37(9):1806-13.
25. Ravikumar C. *Herbal Remedy for Rheumatoid Arthritis. Savitha Dental College*. 2014:310-2.

26. Krocza B, Branski P, Palucha A, Pilc A, Nowak G. Antidepressant-like properties of zinc in rodent forced swim test. *Brain research bulletin*. 2001; 55(2):297-300.
27. Bogdanova OV, Kanekar S, D'Anci KE, Renshaw PF. Factors influencing behavior in the forced swim test. *Physiology & behavior*. 2013; 118:227-39.