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EVALUATION OF ADAPTOGENIC ACTIVITY OF METHANOLIC EXTRACT OF TERMINALIA TOMENTOSA IN EXPERIMENTAL MICE

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Abstract:

The present investigation highlights the effect of Terminalia tomentosa against stress. The effect of Terminalia tomentosa was studied on swim endurance test, anoxia tolerance test, cold restain stress. The active component responsible for this activity may be flavonoid. The present results provide strong evidence that the aqueous extract of barks of Terminalia tomentosa has a definitive anti-stress activity. Mice (20-25 gm) were used. Mice were housed into groups of five under standard laboratory conditions of temperature 25 ± 1ºC with free access to food and water. Terminalia tomentosa extract was dissolved in distilled water and administered orally.

Keywords: *Diazepam (Calmpose) , Ranitidine, Terminalia tomentosa, mice,extract.*

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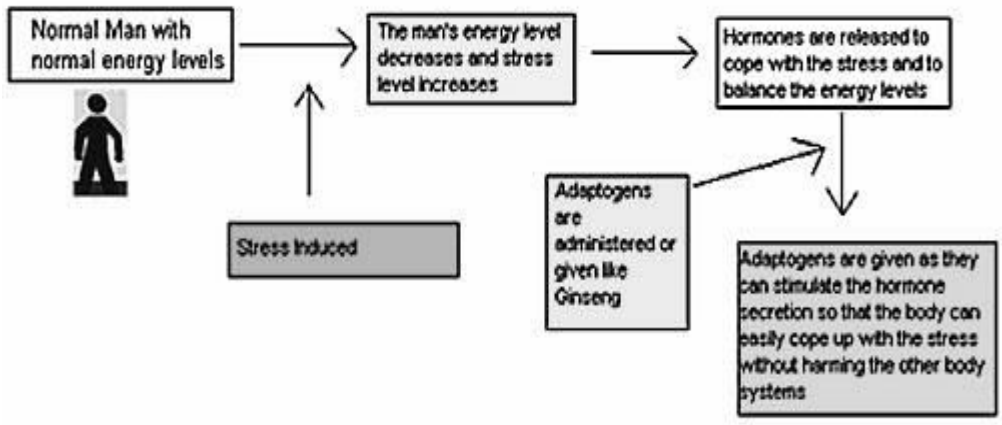
INTRODUCTION:

Natural herb products that supplement the body's ability to deal with stressors such as anxiety, fatigue, or trauma are called adaptogens. In simple terms this ingredient helps the body adapt naturally to cope and with reducing stress. If any person is mentally exhausted or physically fatigued the adaptogens will help him to feel more energetic. The antioxidants contained in the adaptogens help the body fight free radicals which are released during the oxidation process of metabolism in the body, which can cause a variety of problems such as cell degeneration, cancer, ageing and many other diseases. **(Saleby, 2006) (1)**

An increase of over 20% in the capacity to work has been reported as well as a reduction of errors made, by over 80% - which makes this a great nutrient to take when studying, or working at optimum levels. It is further reported that endurance is increased by up to 26% and an increase in strength is improved by nearly 10%.**(Brekhman and Dardymov, 1969) (2)**

Adaptogens are best taken first thing in the morning for best absorption. It has been reported that bodybuilders and athletes improve their performance with adaptogens, since it helps the body to return quicker to its normal resting stage. an action thought to be mediated via the limbic-hypothalamic-pituitary-adrenal axis. The term adaptogen is used by herbalist to refer to a natural herb product that is proposed to increase the body's resistance to stress, trauma, anxiety and fatigue.



Mechanism of adaptogen

Adaptogens are thought to normalize the hypothalamic-pituitary-adrenal (HPA) axis, an intricate system of direct and indirect feedback mechanisms that regulate, most notably, the body's reaction to stress. The HPA axis also plays a major part in the immune system, the process of digestion, energy usage, mood, and sexuality. The HPA is controlled by hormones, the same chemicals that tend to be altered when the body experiences stress .The animals who received the adaptogenic supplement showed smaller changes in plasma corticosterone levels and gastric ulcerations. The experimental group was given standardized extracts of *Schizandra chinesis* and *Bryonia alba*. As compared to the control group, the experimental group showed lower salivary nitric oxide and cortisol levels in saliva after treatment. (Source-www.herbological.com) (3)

Animal models for assessment of adaptogenic activity

The immune system plays an important role in biological adaption, contributing to the maintenance of homeostasis and establishment of body integrity. Hence experimental work related to adaptogenic effect should not only explore the antistress effect but also account for the improvement of defense mechanism of the host. **(Balekar *et al.*, 2006) (4)** Swimming test is test widely used for the measurement of adaptogenic activity. Endurance test is type of swimming test .Physical stress is applied in the form of swimming. **(Bhargava, 1981). (5)**The time is recorded for animal until it got exhausted and drowned this time is referred as swimming time. Another test is described with modifications (five hour swimming test).

In five hour swimming test, physical stress is applied in the form of swimming and increase in weight of adrenal gland and depletion in their ascorbic acid content is noted **(Hazzard, 1983) (6)**.In chronic stress behavioral despair test, mice are forced to swim in a restricted space from which they cannot escape, and are induced to a characteristic behaviour of immobility. When forced to swim in a confined space, mice after an initial phase of vigorous activity, cease to struggle, surrendering themselves to the experimental conditions. This helplessness or despair

behaviour reflected a state of lowered mood in laboratory animals and could serve as a valuable test for screening adaptogenic drugs. **(Borsini and Meli, 1988) (7)**

In chronic stress the phenomenon like depression is induced. Immobility time is increased. There are reports that there is depletion of adrenaline and noradrenaline long with Monoamine oxidase (MAO) level is also decreased during swimming test. Restraint stress has been used in acute and chronic studies, primarily because this stress procedure is very easy. To deliver chronic restraint, animals are usually are placed in a small body sized device for one to several hours of day, and this stress is usually repeated for long period.

Among the recognizable chronic stress models, the chronic mild stress (CMS) model developed by Paul Willner. In the CMS model ,Various mild stresses such as weak noise, cage tilting, wet cage floor, light on during an expected period of darkness, cage shaking etc. are given. This stress treatment is continued for 4-6 weeks . **(Balekar *et al.,* 2006) (8)**

MATERIALS AND METHODS:

1 Animals

Mice (20-25 gm) were obtained from Bharat Serum and vaccines Ltd. Thane, Mumbai. Animals were housed into groups of five under standard laboratory conditions of temperature 25 ± 1ºC with free access to food (Amrut rat and mice feed, Sangli, India.) and water. The experiments were performed during the light portion (12-12 h). The experiments were carried out according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India and approved by the Institutional Animal Ethical Committee.

2 Drugs and chemicals

Diazepam (Calmpose) was purchased from Ranbaxy, Mumbai. Ranitidine, *Terminalia tomentosa* extract was dissolved in distilled water and administered orally.

3 Preparation of extract

From Bark of *Terminalia tomentosa* (200 gm) was purchased from the local market and then bark were dried and then the powdered *Terminalia tomentosa* was macerated with the water for 2 days. Then filtration was carried out. Extract was concentrated and evaporated to dryness for getting the crude aqueous extract *Terminalia tomentosa* (T.T) (Yield: 9.2% w/w).

Methods

1. Swim endurance test

Swiss albino mice (25 ± 2 gm) of either sex were used. Seven groups (n=5) were prepared. The control animals were orally treated with distilled water 10ml/kg, per oral (p.o.) as vehicle for 14 days. Five groups were orally treated with ST (10 mg/kg, 30 mg/kg and 100 mg/kg), EAF (10 mg/kg and 30 mg/kg) respectively for 14 days. The Diazepam (Calmpose) was used as standard at the dose of 1 mg/kg intraperitoneally (i.p). On day 14, mice were allowed to swim in cylindrical container filled with water maintained at 25 ± 2°C, till they got exhausted and the time they drowned was considered as end point (swimming time). **(Nimbakar *et al.,* 2001). (9)**

2. Anoxic stress tolerance test

Swiss albino mice (25 ± 2 gm) of either sex were used. Seven groups (n=5) were prepared. The control animals were orally administered with distilled water (10ml/kg, p.o) as vehicle for 14 days. Five groups were orally treated with ST (10 mg/kg, 30 mg/kg and 100 mg/kg), EAF (10 mg/kg and 30 mg/kg) respectively for 14 days. The Diazepam (Calmpose) was used as standard at the dose of 1 mg/kg i.p. On day 14, 1h after the treatment, each animal was placed in airtight 250 ml conical flask. The time duration from the entry of the animal in the conical flask to the appearance of the first convulsion was noted as anoxic stress tolerance time . **(Tomar *et al.,* 1984). (10)**

3.Cold restrain stress in mice

Swiss albino mice (25 ± 2 gm) of either sex were used. Seven groups (n=5) were prepared. Group 1st and 2nd were treated extract of *Terminalia tomentosa* 0.1 and 0.3 respectively using oral gague, for 7 days. Group 3rd mice were administered std drug diazepam (1mg/kg i.p.). On the 8th day, animals were individually placed in plastic containers of capacity 350 mL. they were immobilized in their normal position, using adhesive tape. The containers were placed in a freeze for 2 h. the blood was collected by heart puncture method, in a heparinised tube and WBC count was done, blood glucose level was determined.

RESULTS:

1. Swim Endurance test

Animals treated with vehicle showed 200.8 ± 8.693 min as swimming time. Groups treated with TT (0.1, 0.3 mg/kg p.o) showed significant ($P<0.05$) increase in swimming time as compared to control group (Fig 1 and Table 1).

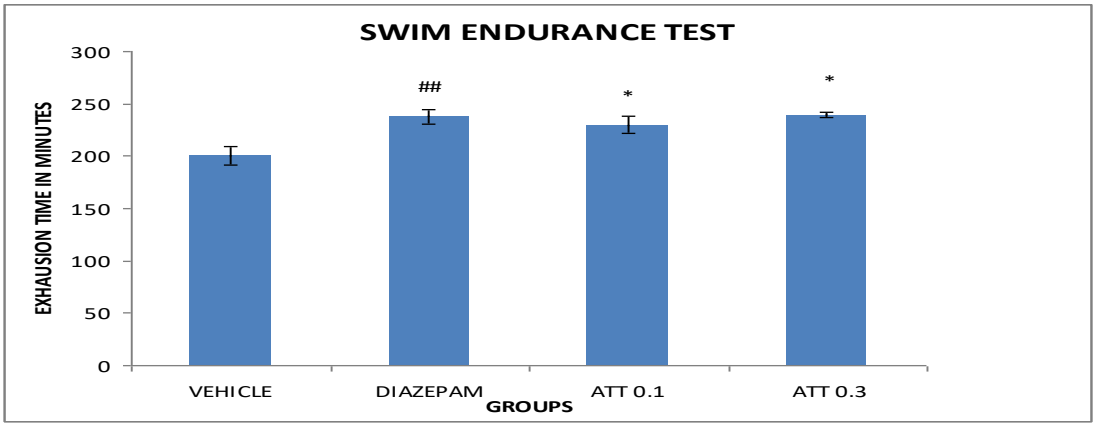


Fig 1:-Effect of aqueous extract of TT (0.1, 0.3 mg/kg) on swim endurance test in mice. All values are expressed as mean ± SEM, n=5. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group. Vertical lines represent S.E.M. TT-*Terminalia tomentosa* DZP-Diazepam,

Table 1:- Effect of *Terminalia tomentosa* on Swim endurance test in mice.

n=5, all values are expressed as mean ± SEM. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group.

Where,

TT = *Terminalia tomentosa*

Sr.no	Treatment group	Swimming time (min)
1	Control	200±8.693
2	Diazepam (1 mg/kg)	238 ± 7.11*
3	TT (0.1 mg/kg)	230± 7.616*
4	TT (0.3 mg/kg)	240± 2.462*
F value		8.61

2. Anoxic stress tolerance test

Animals treated with vehicle showed 45.75 ± 0.85 min as anoxic stress tolerance time. Groups treated with TT (0.1, 0.3 mg/kg p.o) showed significant (P<0.05) increase in anoxic stress tolerance time as compared to control group (Fig 2, Table 2).

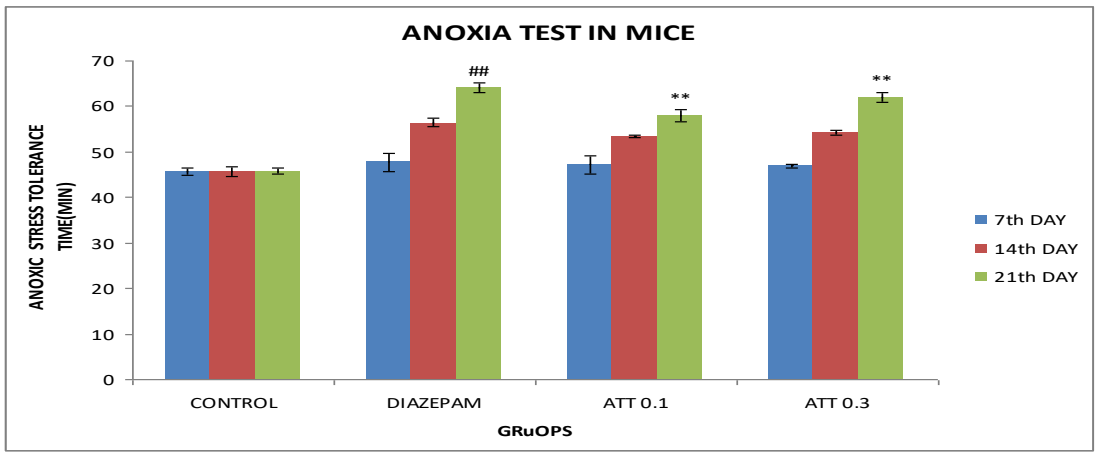


Fig 2-Effect of aqueous extract of TT (0.1, 0.3 mg/kg) on Anoxic stress tolerance test in mice. All values are expressed as mean ± SEM, n=5. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group.

Table 2:-Effect of aqueous extract of *Terminalia tomentosa* bark on Anoxic stress tolerance test in mice n=5, all values are expressed as mean ± SEM. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group.
Where,

TT=*Terminalia tomentosa*

Sr.no	Treatment group	Anoxic stress tolerancetime (min)		
		7th day	14th day	21st day
1	Control	45.75 ± 0.85	45.5±1.041	44.5±0.64
2	Diazepam (1 mg/kg)	47.75 ± 0.016*	56.5±0.95	64±1.08
3	ST (0.1 mg/kg)	47.25±2.016	53.5±0.28	58.25±1.25
4	ST (0.3 mg/kg)	47± 0.40	54.25±0.62	62±1.08
F value				

3. Cold restrain stress in mice

Animals treated with vehicle showed 5525 ± 197cumm-1 of cholesterol level as cold restrain stress. Groups treated with TT (0.1, 0.3 mg/kg p.o) showed significant (P<0.05) decrease in a cholesterol level compared to +ve control group (Fig 3, Table 3).

Sr.no	Treatment group		
		Total WBC count(cell cumm -1)	Blood glucose level
1	Normal	5525±197.4	81.61±0.4
2	Control	6625±303.1	125±0.06
3	Diazepam (1 mg/kg)	5662±207.5	89.7±0.60
4	ST (0.1 mg/kg)	5262±303	95.21±0.36
5	ST (0.3 mg/kg)	5420±228.9	90.8±0.36
F value			

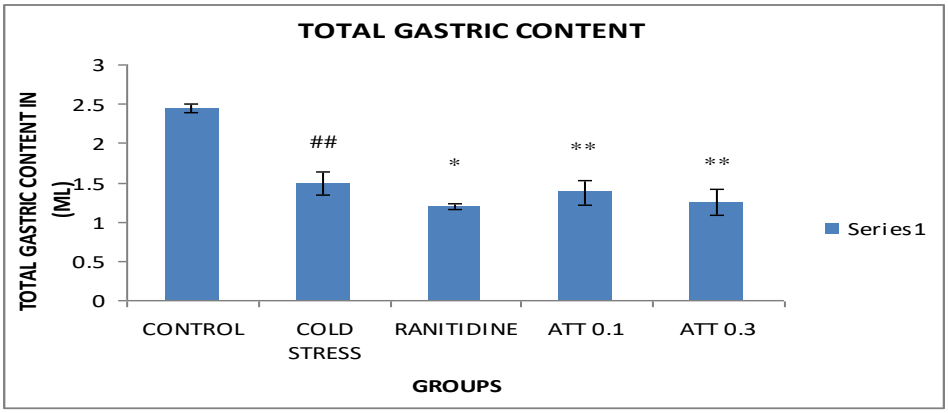


Fig .3:-Effect of aqueous extract of TT (0.1, 0.3 mg/kg) on cold restrain stress in mice. All values are expressed as mean ± SEM, n=5. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group

Animals treated with vehicle showed 81.61 ± 0.4mg/dl as cold restrain stress of blood glucose level. Groups treated with TT (0.1, 0.3 mg/kg p.o) showed significant (P<0.05) decrease in a cold restrain stress tolerance time as compared to +ve control group (Fig 3, Table 3).

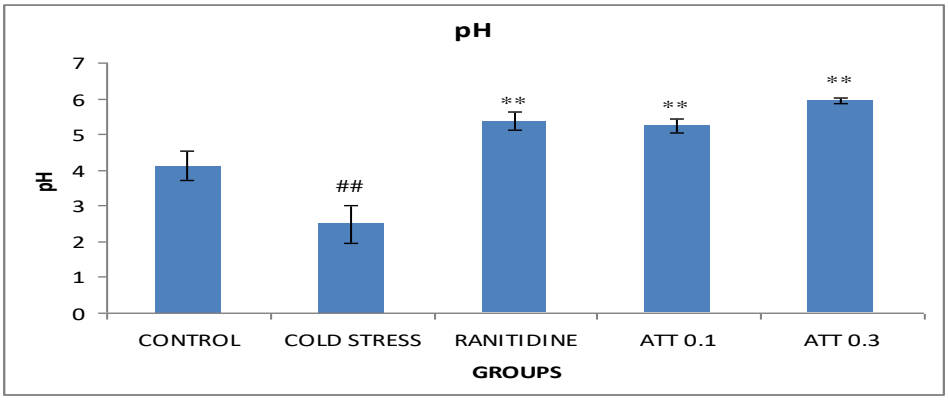


Fig 4-Effect of aqueous extract of TT (0.1, 0.3 mg/kg) on cold restrain stress in mice. All values are expressed as mean ± SEM, n=5. All data were subjected to One Way ANOVA followed by Dunnett's test.*P<0.05 was considered significant as compared to control group.

DISCUSSION:

In present study the phytochemical screening of aqueous extract *Terminalia tomentosa* barks revealed presence of alkaloids, flavonoids, saponins, tannins and glycosides. Swim endurance test is the model for measurement of Swimming time. Swim endurance test is useful in determination of swimming performance. This test is not generally used because it is time consuming and there may be chances of death of animal. Endurance is defined as the ability to repeat muscular contractions without fatigue. Fatigue is a decline in level of performance. The performance relates to muscular contractions and dependant on energy sources. In swim endurance test, stress is applied by means of swimming. The end point is the time at which it got exhausted and drowned, this time is referred as swimming time. The animal is allowed to swim in cylindrical container till its end point. There are reports that plasma levels of adrenaline and nor-adrenaline are enhanced whereas the levels of MAO are reduced during stress induced by swim endurance test . It has been reported earlier that, *Tribulus terrestris* significantly increased swimming time and shown significant adaptogenic property, it may be possibly normalizing the plasma levels of catecholamines and MAO Pretreatment with the ST (10, 30 and 100 mg/kg) and EAF (10 and 30 mg/kg) has increased swimming time. The swimming time was increased in dose dependant manner.

Anoxic stress tolerance test is sensitive to level of oxygen present in conical flask. As the volume of conical flask is increased, oxygen level also increased. This increased volume indirectly affects time of onset of convulsion. In anoxic stress tolerance test, anoxia is a very severe stressor. All the body functions, including cellular respiration depends on the oxygen supply to them. Lack of this vital element will cause all the body functions to cease. Increase in adaptation during this stress by any drug could be considered as Adaptogenic effect .It has been reported earlier that, when mice are subjected to this hypobaric environment for specified period , the mitochondria of heart and brain cells of mice are seriously damaged and brain neurotransmitters i.e. norepinephrine (NE), dopamine (DA), serotonin (5-HT), acetylcholine (Ach), are significantly decreased .In this model, a mouse is kept in 250 ml conical flask. The end point is onset of convulsion.

It has been reported earlier that, *Triphala formulation* has significantly increased anoxic stress tolerance time. This effect of *Triphala formulation* may be related to an increase in the cerebral resistance to anoxia and reducing the cerebral consumption of oxygen in anoxic stress. The protective action on anoxic stress mice may be due to action on pituitary adrenal gland axis. *Tribulus terrestris* also increased anoxic stress tolerance time. In our study, Pretreatment with ST (10, 30 and 100 mg/kg) and EAF (10 and 30 mg/kg) significantly increased the anoxic stress tolerance time in mice in dose dependant manner. It is also suggested that adaptogenic agents facilitate the conversion of energy in the cellular system of the organism and helps in adaptation

CONCLUSIONS:

The present investigation highlights the effect of *Terminalia tomentosa* against stress. The effect of *Terminalia tomentosa* was studied on swim endurance test, anoxia tolerance test, cold restain stress. The active component responsible for this activity may be flavonoid. The present results provide strong evidence that the aqueous extract of barks of *Terminalia tomentosa* has a definitive anti-stress activity.

In conclusion, our data shows that *Terminalia tomentosa* has adaptogenic activity possibly due to inhibition of release of inflammatory mediators and T cell activation; and modulation of sympathetic pathway.

REFERENCES:

1. Saleby JP. (2006). Adaptogenic Potential of a Polyherbal Natural Health Product. *Evid Based Complement Alternat Med,* 4(3): 375–380.
2. Brekhman II and Dardymov IV. (1969). New substances of plant origin, which increases nonspecific resistance. *Ann.Revised .Pharmacol*, 9:419-21.
3. www.herbological.com
4. Balekar N.S, Bodhankar S.L and Jain D.K. (2006). Screening methods for Immunomodulatory agents –A Review. *Indian drugs*, 43 (7), 325.
5. Bhargava KP and Singh N. (1981). Antistress activity of Ocimum sanctum, *Indian J Med Res*, 73:443-51.
6. Hazzard WR. (1983). The biology of ageing in Harrison's principle of Internal medicine, McGraw Hill, 418-422.
7. Borsini F, Meli A (1988) is the forced swimming test a suitable model for revealing antidepressant activity? Psychopharmacology 94:147–160
8. Balekar N.S, Bodhankar S.L and Jain D.K. (2006). Screening methods for Immunomodulatory agents –A Review. *Indian drugs*, 43 (7), 325.
9. Nimbakar SR, Patki VP, Patki MP. (2001).Pharmacological evaluation of antitstress& androgenic activity of polyherbal formulation AP-3000 containing Panax ginseng. *Indian Drugs*, 38: 27-39.
10. Tomar VS, Singh Sp, Singh N. (1984). Antistress activity of a gem containing Unani formulation.Indian drugs, 3:233-235.