JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

An Acute oral Toxicity Study of T-AYU-HMTM on Swiss Albino Mice

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ABSTRACT:

Sickle cell anemia is an autosomal recessive type of hemoglobin disorder with which every year 300000 children are born. In sickle cell anemia reduced life of red blood corpuscular the devastating and life threatening clinical sign and symptoms can occur in patients. Therefore the management is major health concern. The main intend or current challenge has always been to improve the clinical aspects of quality of life of the patients with low toxicity and safer and easy to administer therapy. T-AYU-HMTM is a novel timely tested anti-sickling Traditional Ayurvedic Medicine designed on such a purpose to reduce clinical complications and enhance the quality of life. The present study is single dose oral toxicity study of T-AYU-HMTM was performed to assess its Safety profile at high dose. Various parameters like Body weight, mortality, and clinical signs of hematological parameters were assessed. Results show that T-AYU-HMTM is safe up to the dose level of 2000mg/kg body weight.

KEY WORDS: Sickle cell anemia, Anti-sickling, oral toxicity study, traditional medicine, T-AYU-HMTM

Article history:

Received 09 Sept 2015
Revised 02 Oct 2015
Accepted 05 Oct 2015
Available online 15 Oct 2015

Citation:

Desai A. M., Desai C., Desai H. An Acute oral Toxicity Study of T-AYU-HMTM on Swiss Albino Mice. **J Pharm Sci Bioscientific Res**. 2015 5(5):504-507

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INTRODUCTION:

Sickle cell anemia is an Autosomal Recessive disorder which affects almost 300000 children born affected by this hemoglobin disorder.1 It is most commonly pronounced in poor countries located in subtropical regions, in India most commonly the tribal areas are mostly suffered from this condition.2, 3 Clinical features of this conditions are common like fever, cough, abdominal pain, pallor, dizziness, giddiness, weakness, fatigue can be devastating if remain undiagnosed or untreated. Crisis because of Pain which main symptom I sickle cell anemia are characteristics observation in patients of sickle cell anemia.4-7 As far as management is concern because of inadequate diagnosis and available treatment it is the major health concern. Secondary if we look at genetic bases it is autosomal recessive type so any drug designed by must be keeping the points in mind that it would have to be tolerated throughout the life by the patients with low toxicity and easy avaibility and affordability.8 Since last many years scientific clinical research and development claiming that gene therapy and bone marrow transplantation can cure the condition but the question arise in mind that with how many patients can benefited from it and who can afford it? One such hope oral administer therapy is hydroxyurea which no doubt has been proved to be safe for long term use, however it has been reported that hydroxyurea has mixed effects on erythroid precursors, depending on the genotypic

variation and all the patients do not respond equally well to hydroxyurea.[9-11]

So with emphasizing on timely tested Ayurvedic traditional medicine which has been the strength of our country can be used in this kind of hereditary disorder will be needed to design. WHO has also stated that systematic gathering of information on the most cost-effective approaches for the prevention and treatment should be promoted.[12] Therefore, T-AYU-HM™ is a novel anti-sickling Traditional Ayurvedic Herbo-mineral medicine designed to enhance the quality of life and reduced the painful complications in patients of sickle cell anemia. As we know that WHO has also appreciated the importance of medicinal plants for the public health care in developing nation and for that evolved the guidelines to support and formulate national policies on traditional medicine to study their potential usefulness including evaluation and safety and efficacy parameters.

MATERIALS AND METHODS:

Single dose oral toxicity of T-AYU-HM™ was performed as per the OECD guideline number 423 to assess its safety profile at high dose. 3 animals were used for control and for each dose level (300, 2000 & again 2000mg/kg (to nullify the error) respectively). The period for the observation of the study was for 14 days. All animals were observed for the change in body weight, clinical signs and mortality especially for first four hour after the dose administration of the drug and subsequently twice a day during 14 days of time period. On 14th day, blood was collected by puncturing the supra-orbital plexus by capillary tubes under ether anesthesia for the estimation of hematological parameters. To estimate complete blood profile 0.08ml blood sample was mixed with 0.02 ml of EDTA and fed to the auto analyzer. The parameters measured were as follow total red blood corpuscles, mean corpuscle hemoglobin, mean corpuscle hemoglobin concentration, mean corpuscle volume, white blood cells, Neutrophils, lymphocyte, Eosinophil, monocyte, platelets count and packed cell volume.

Animals: All female Swiss albino mice ranging from 25-30 gm weight were screened from the animal house. 3 animals in each group were housed in separate cage. The dry wheat waste was used as bedding material and it was changed every day. The animals were acclimatized for seven days before commencement of the experiment in standard laboratory conditions The animals were housed under standard condition and room temperature which was maintained around 25±3°C, 12 ± 01 hour day and night rhythm, and the humidity was maintained between 40 to 60%. For their drinking purpose, tap water ad libitum was used. The study was performed at Smt. B.N.B Swaminarayan Pharmacy College animal house as per the OECD 423 guideline approved by the institutional animal ethics committee.

Table1: group of mice in experiment

group	Formulation	Dose(mg/kg)	Animal no
C1	Control	0	1-3
T1	T-AYU-HM™	300	4-6
T2		2000	7-9
T3		2000	10-12

Statistical analysis: The results were presented as Mean ± SEM for three rats in each group. Student t-test with P< 0.05 was used for statistical comparison.

Results: In the acute toxicity study no mortality was observed in treated rats and no toxic effect was observed throughout the 14 days study period at a dose of 2000 mg/kg in the test sample of T-AYU-HM™ tablet. There were no changes observed in normal gross behavior of animals in the treated groups. There were no significant changes in body weight of the treated and control rats have been shown in Table 2. None of the hematological parameters was affected to significant extent in the sample of T-AYU-HM™ tablet in comparison to control group Table 3.

Table 2. Change in Body weight at the end of study.

Group	Dose	Body weight(gm)		
		Day 0	**Day 7**	**Day 14**
C	0	28.66±0.73	30.17±0.73	31.83±0.60
T1	300	30.33±1.92	31.50±1.76	32.33±1.42
T2	2000	31.50±0.76	32.67±0.60	33.33±0.44
T3	2000	30.33± 1.20	31.83±1.42	33.00±1.26

The mean body weight observed in (±SEM) of each group treated with T-AYU-HM™ were present in above table. No significant changes were observed in body weight of test sample treated groups.

Table 3: change in hematological parameters

Parameters		C1 (Control)	T1 (300 mg/kg)	T2 (2000 mg/kg)	T2 (2000 mg/kg)
WBC (K/µl)	Mean (SD)	4.67 (0.87)	6.37 (0.55)	6.67 (0.57)	6.50 (0.96)
RBC (M/µl)	Mean (SD)	8.54 (0.23)	8.25 (0.81)	8.47 (0.57)	8.49 (0.37)
Hb (g/dl)	Mean (SD)	15.40 (0.66)	14.13 (1.53)	14.77 (0.85)	14.80 (0.46)
Hct (%)	Mean (SD)	41.30 (1.80)	42.07 (4.71)	43.07 (2.23)	43.10 (2.00)
MCV (fl)	Mean (SD)	48.37 (1.16)	50.93 (1.42)	50.90 (0.92)	50.77 (0.31)
MCH (g/dl)	Mean (SD)	18.07 (0.38)	17.13 (0.21)	17.47 (0.58)	17.43 (0.23)
MCHC (g/dl)	Mean (SD)	37.27 (0.21)	33.60 (1.08)	34.30 (0.80)	34.37 (0.57)
PLT ($\times 10^3$/µl)	Mean (SD)	809.33 (90.39)	872.67 (115.08)	734.67 (88.10)	696.33 (82.60)

(Data are Mean and SD (standard deviation) of 3 animals, student's t-test at 0.05)

DISCUSSION:

The drugs intended to be used therapeutically should be subjected to toxicity evaluation before they are considered safe for use in the human beings. This study is important because incomplete knowledge about the toxicity profile of a putative drug will entail certain amount of risk to the recipient. According to the system of global harmonization of Chemicals, this product is classified in Category 5 which is the higher lethal dose 50 is 2000 mg/kg. Toxicological research and testing helps to live safely and to derive benefit from natural and synthetic substances. In this study no changes attributable to treatment were found in body weight and any macroscopic changes that could point to the cause of the death observed up to the maximum dose of 2000 mg/kg (BW) of the drug sample.

Conclusion:-

From the observations recorded during acute oral toxicity study for behavioral changes, hematological parameters, changes in body weight and mortality, it was clear that the sample of T-AYU-HM^{TM} a novel Herbo-mineral anti-sickling traditional Ayurvedic medicine was relatively safe.

ACKNOWLEDGEMENT:

The authors would like to thank the Principal Dr. Anil Jadhav of Smt.BNB. Swaminarayan Pharmacy College for allowing conducting the work fluently and providing facility for the work.

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