IJPSR (2020), Volume 11, Issue 12 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 November 2019; received in revised form, 27 February 2020; accepted, 11 March 2020; published 01 December 2020

AN ACUTE ORAL TOXICITY STUDY OF T-AYU-HM PREMIUM TABLET IN RATS: AN INITIATIVE FOR SICKLE CELL ANEMIA MANAGEMENT

Atul M. Desai [*1], Hemshree Desai [2], Chirag Desai [3] and Manish Patel [4]

Dhanvantari Clinic [1], Ayurveda Health Care and Research Center, Shreeji Desai Market, Vyara - 394650, Gujarat, India.
Shree Sardar Smarak Hospital [2], Bardoli, Surat - 394601, Gujarat, India.
Smt. BNB. Swaminarayan Pharmacy College [3], Salvav - 396191, Gujarat, India.
Department of Toxicology [4], Jai Research Foundation, Vapi, Valvada - 396105, Gujarat, India.

Keywords:

Sickle cell anemia,
OECD, T-AYU-HM Premium

Correspondence to Author:
Dr. Atul M Desai

Principal Investigator,
BAMS, FIIM, Ph.D. (MUHS),
Dhanvantari Clinic, Ayurveda Health Care and Research Center, Shreeji Desai Market, Vyara - 394650, Gujarat, India.

E-mail: dratuldesai@rediffmail.com

ABSTRACT: Sickle cell anemia is a major life-threatening hemoglobin disorder in the world. This hemoglobin disorder is an autosomal recessive type, therefore considered as a major health problem in the world. The pain symptoms and complications of sickle cell anemia can be life-threatening many times. Management of sickle cell anemia demands drugs to be safe, well-tolerated, lesser side effects, and effective in improving the quality of life in patients. The alternative system of medicine can be the fruitful therapeutic option in conditions where the drug has to be consumed for life long. The T-AYU-HM Premium is a novel traditional Ayurvedic medicine designed on such a purpose to reduce clinical complications and enhance the quality of life in sickle cell anemia patients. The study conducted was a single dose oral toxicity study of T-AYU-HM Premium to assess its safety profile at a high dose. The study was conducted in compliance with the OECD principles of GLP (1998). The study was conducted according to OECD for testing of chemicals, N-425 acute oral toxicity Study–Up and Down Procedure. Various parameters, like mortality, clinical signs, and Bodyweight, were assessed. Results show that T-AYU-HM Premium is safe for greater than 5000 mg/kg body weight. No signs of mortality or clinical parameter changes were observed. No significant body weight changes were observed in the study. The results suggest that T-AYU-HM Premium might become a good therapeutic option for sickle cell anemia in the future.

INTRODUCTION: Sickle cell anemia is a genetic (autosomal Recessive) disorder that affects almost 5% of the world population. Based on the 1981 census in India, it was projected that there were 24, 34,170 sickle cell trait and 1, 21,375 sickle cell disease patients amongst the tribal area in India. As per the 2011 census 1, 78, 62,455 are sickle cell trait and 13, 39,684 sickle cell disease amongst the tribes in India.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(12).6157-60

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(12).6157-60

This data suggest that hemoglobin disorder is a major health issue of tribal population, which is restricting them from becoming grow and developed. Not only India, but studies reported that over two million Americans are the carrier of the sickle cell gene [1-7].

World health organization has mentioned that organized gathering of information on the most cost-effective approaches for the prevention and treatment should be promoted. World health organization has also emphasized the importance of medicinal plant's role in public health care, especially in developing nations. Therefore, proper guidelines and policies on standardized the potential of traditional medicines are designed to evaluate safety and efficacy parameters.

As per previous literature, it was already observed that more number of patients prefer an alternative system of medicines for the management of sickle cell pain full crisis. T-AYU-HM Premium is a novel anti-sickling traditional ayurvedic herbomineral medicine designed to enhance the quality of life and reduced the painful complications in patients of sickle cell anemia. The *in-vitro* study data suggest the potential of drug be used in the management of sickle cell anemia [7-10].

T-AYU-HM Premium is a novel formulation made up of extract of eight Indian origin herbal plants and two purified minerals. *In-vitro* anti-sickling effect of T-AYU-HM Premium was evaluated at the Bombay College of Pharmacy Kalina, Mumbai. The results showed that T-AYU-HM Premium had a potent anti-sickling effect on sickle erythrocytes obtained from patients with sickle cell disease [9].

MATERIALS AND METHODS: [11-13]

Study Objective: The study was performed to assess the acute oral toxicity (LD_{50}) study of T-AYU-HM Premium tablets in Wistar rats. The study was conducted in compliance with the OECD principles of GLP (1998).

Study Guideline: The study was conducted according to OECD for testing of chemicals, N-425 "Acute Oral Toxicity Study–Up and Down Procedure".

Justification of Selection System: The rat (*Ratus norvegicus*) was selected as the test system because it is a readily available rodent species. It has been historically shown to be a suitable model for acute oral toxicity assessment and is recommended by OECD and other regulatory authorities.

Study Duration and Protocol Number: The study was performed in 2013-14 and the protocol number 401-1-01-7912.

Acclimatization: The rats were received into the experimental procedure room and allowed to acclimatize for a period of 6 days for rat number 1, 8 days for rat number 2, 10 days for rat number 3, 12 days for rat number 4, 14 days for rat number 5 and 16 days for rat number 6 prior to dosing.

Feed and Water: The rats were provided with feed and water *ad libitum.* The quality of feed and water is regularly monitored.

Environmental Conditions: The temperature range was 19-23 degrees Celsius. The relative humidity range was between 64-66%.

Observation: The rats were observed for sign of toxicity and mortality at 30 min, 1 h, 2 h, 3 h, 4 h, and 6 h post-dosing on the day of dosing. Subsequently, the rats were observed twice a day for morbidity and mortality for a period of 14 days following oral dosing. The clinical signs were recorded once a day. Individual body weight was recorded prior to dosing on day 0 and day 7 and day 14 following oral dosing. At the end of 14 days period, all rats were euthanized for pathological examination.

RESULTS: No mortality was observed in all the rats treated at the dose level of 175 mg, 550 mg, 1750 mg, and 5000 mg T-AYU-HM Premium tablets/kg body weight.

TABLE 1: DOSE, MORTALITY/ANIMALS TREATED

S. no.	Dose (mg/kg body weight)	Female rat (mortality/total)
1	175	0/1
2	550	0/1
3	1750	0/1
4	5000	0/1

No sign of toxicity was observed in all the rats treated at dose level of 175 mg, 550 mg, 1750 mg, and 5000 mg T-AYU-HM Premium tablets/kg body weight throughout the experimental period.

TABLE 2: INDIVIDUAL CLINICAL OBSERVATION AND MORTALITIES

Rat number	Dose (mg/kg body weight)	At hour (day 0)						On day													
		1	2	3	4	5	6	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	175	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	550	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3	1750	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4	5000	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5	5000	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6	5000	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

1 = Normal and Day 0 = day of dosing.

There was a normal gain in body weight of all the rats during the experimental period.

TABLE 3: BODY WEIGHT (g) AND PERCENT BODY WEIGHT CHANGES OF INDIVIDUAL RAT

Rat number	Dose	Bodyweight on day			Percentage of body weight change on day	
		0	7	14	7	14
1	175	180.1	193.0	204.1	7.16	13.33
2	550	174.2	186.1	195.7	6.83	12.34
3	1750	174.8	187.0	196.9	6.98	12.64
4	5000	191.2	207.1	215.8	8.32	12.87
5	5000	194.1	202.2	211.1	4.17	8.76
6	5000	193.0	207.4	218.2	7.46	13.06

0 = before dosing, sex = female rats.

Microscopic findings of an external examination of the terminally sacrificed rats did not reveal any lesion of pathological significance, and visceral examination of rats sacrificed at termination did not reveal any lesion of pathological significance.

In the absence of any pathological lesion in sacrificed rats, it is concluded that the test item did not produce any treatment-related effect at the dose level used in the study.

TABLE 4: NECROPSY FINDINGS OF INDIVIDUAL RAT

Rat number	Dose (mg/kg body weight)	Mode of death	External	Internal
1	175	Terminal sacrifice	No abnormality detected	No abnormality detected
2	550	Terminal sacrifice	No abnormality detected	No abnormality detected
3	1750	Terminal sacrifice	No abnormality detected	No abnormality detected
4	5000	Terminal sacrifice	No abnormality detected	No abnormality detected
5	5000	Terminal sacrifice	No abnormality detected	No abnormality detected
6	5000	Terminal sacrifice	No abnormality detected	No abnormality detected

The LD_{50} was found to be greater than 5000 mg T-AYU-HM Premium tablet/kg body weight. Since the value was found to be greater than 5000 mg/kg body weight, T-AYU-HM Premium is being classified as “unclassified” as per the globally harmonized system of classification and labeling of chemical (GHS 2013).

CONCLUSION: From the study, observations of clinical parameters, body weight, and mortality rate it was concluded that the Herbo–Mineral formulation T-AYU-HM Premium is safe and might become a potential therapeutic option for management of sickle cell anemia.

ACKNOWLEDGEMENT: The authors would like to express their sincere thanks to Jai Research Foundation, Vapi, for the study.

CONFLICTS OF INTEREST: The authors would also express there is no conflict of interest for the study.

REFERENCES:

1. National rural health management program, sickle cell anemia control program, from http;//www.nrhm.gujarat.gov.in/sickle-cell.htm
2. World Health Organization Report: Community control of hereditary anemias. Memorandum from world health organization meeting: Bull World Health Organ 1983; 61: 63-80.
3. Rao VR: Genetics and epidemiology of sickle cell anemia in India. Indian Council of Medical Research Bull 1988; 18: 87-90.
4. Malhotra KC: Genetico-environmental disorders and their impact on mortality and morbidity profile among tribal population. In: Basu S K (Ed) Tribal Health in India. New Delhi: Manak Publishers 1993.
5. Sickle Cell Disease Association of America. 2013. Sickle cell disease is a Global Public Health Issue. Available at: http://www.sicklecelldisease.org/index.cfm?page=scd-global
6. Desai C, Desai J, Desai S and Kajal K: A brief review on the management options available for sickle cell anemia. Journal of Pharmaceutical Science and Bioscientific Research 2015; 5(2): 230-38.
7. Desai AM, Desai C and Desai H: An Acute oral Toxicity Study of T-AYU-HMTM on Swiss Albino Mice. Journal of Pharmaceutical Science and Bioscientific Research 2015; 5(5): 504-07.
8. World Health Organization, 59th World Health Assembly. Sickle Cell Anemia, report by Secretariat. 2006. [Last Accessed on 2011 June]. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA59/A59_9-en.pdf.
9. Desai A and Desai K: Efficacy of poly herbo-mineral formulation T-AYU-HM™ on sickle cell diseases from ayurveda. International Journal of Current Research 2016; 8 (4): 29829-31.
10. World Health Organization. Health of indigenous peoples. Geneva, Switzerland: Factsheets N° 326; 2007.
11. OECD 1998: OECD Environmental health and safety publications series on principles of good laboratory

practice and compliance monitoring, number 1, "OECD Principles of Good Laboratory Practice." ENV/MC/CHEM (98)17(as revised in 1997)

12. OECD 2008: OECD N-425 "Acute Oral Toxicity Study – Up and Down Procedure" The OECD guideline for testing of chemicals, adopted by the council on October 03, 2008.
13. United nations 2013: GHS ST/SG/AC.10/30/ revised 5. Globally harmonized system of classification and labeling of chemical (GHS) - 5th revised edition, United Nations, New York and Geneva. ISBN-978-92-1-117067-2

How to cite this article:
Desai AM, Desai H, Desai C and Patel M: An acute oral toxicity study of T-AYU-HM premium tablet in rats: an initiative for sickle cell anemia management. Int J Pharm Sci & Res 2020; 11(12): 6157-60. doi: 10.13040/IJPSR.0975-8232.11(12).6157-60.

All © 2013 are reserved by the International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **Android OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)