

CYTOPROTECTIVE ACTIVITY OF ASHWAGANDHA SIDDHA GRUTHA AGAINST CYCLOPHOSPHAMIDE INDUCED TOXICITY IN WISTAR RATS AN EXPERIMENTAL STUDY

Goutham S. P. Janthli Deepa Manjunath Swarna Latha Srinivas Datar
Dept. of Agada Tantra, S. D. M. College of Ayurveda, Hassan, Karnataka, India

ABSTRACT

Ashwagandha is a plant which has drawn the interest of many researchers in several countries, either for its active principle or for the extremely important pharmacodynamic or pharmacotherapeutic properties. Although great advances were made in modern medical science to control disease but many diseases like cancer are not yet curable fully. The underlying mechanism leading up to cancer are still unknown and cancer remains a mystery disease. The present study was undertaken to evaluate the effect of immunomodulatory activity *Ashwagandha siddha Grutha* in Cyclophosphamide induced cell toxicity in Wistar rats. The *Ashwagandha siddha Grutha* provided significant increase in concentration of Haemoglobin by 1.31%, Total count 27.75%, RBC by 2.30%, Platelet count by 9.56%. It also produced significant decrease in concentration of SGOT by 28.39%, SGPT by 3.58%, Urea by 35.88%, Creatinine by 29.68%. *Ashwagandha*'s chemopreventive properties make it a potentially useful adjunct for the patients undergoing radiation and chemotherapy.

Keywords: *Ashwagandha*, Cyclophosphamide, Wistar rats, *Ashwagandha siddha Grutha*, Cancer, Immunomodulatory

INTRODUCTION

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries.¹ Cancer is a major public health concern in India and has become one of the ten leading causes of death in the country. It is estimated that there are about 28 lakh cases of cancer at any particular point of time with 10 lakh new cases occurring every year. About 5 lakh deaths occur annually in the country due to cancer. As per WHO Report 2005, the estimated Cancer Deaths in India is projected to increase to 7 lakh by 2015². The prevalence of cancer in India is

estimated to be around 2.5 million, with over 800,000 new cases and 550,000 deaths occurring each year due to this disease in the country.³

Chemotherapy is the primary treatment available for disseminated malignant disease, most common chemotherapy agents which acts by killing the cells that divides rapidly, one of the main properties of cancer cell. This means chemotherapy also harms the cells that divide rapidly under normal circumstances in bone marrow.⁴

Immuno suppression is the major drawback in chemotherapy and it also has the toxic side effects like myelosuppression,

mucosal ulceration and alopecia etc.⁵ Cyclophosphamide is one of the most widely used broad spectrum antitumor agent. It is used in the treatment of carcinoma of breast, lungs, ovary, bladder, non Hodgkin's, acute and chronic leukemia etc.

Cyclophosphamide itself is carcinogenic. It potentially has ability to cause transitional cell carcinoma of bladder as a long term complication. It can lower the body's ability to fight an infection causing Immuno suppression and also have side effects like bone marrow toxicity and testicular cell damage.⁶

Cytoprotection means protection of cell from noxious chemicals or other stimuli or enhancing the ability of cell to resist injury.⁷ Cytoprotective agents will reduce or prevent the toxicities. The Cytoprotective agents should ideally be selective for normal cell versus cancer cells. They should have no negative impact on anticancer therapy and have minimal adverse effect.⁸

In all types of *Vishas* and in all stages of *Vishas*, *Grutha* is said to be *sreshtha*.⁹ It is believed to be best for human consumption since it is full of nutritive properties, and is considered as good *Vishagna* (Antitoxic) and *Ashwagandha* have the properties like *Vishagna* (Antitoxic).¹⁰ *Ashwagandha* has been used for a very long time for all age groups and

RESULTS

Table 1: Effect of *Ashwagandha siddha grutha* on Haemoglobin concentration

Group	Haemoglobin (unit) MEAN ± SEM	% change
Control(tap water 5ml/kg)	16.07 ± 0.32	-
Cyclophosphamide control 6mg/kg/BW	15.16 ± 0.14*	5.66 @
Ashwagandhasiddagrutha 4.5ml/kg/BW	15.36 ± 0.24	1.31 #

*P<0.05 in comparison to normal control group, @- Compared with normal control # - compared with Cyclophosphamide control.

both sexes,¹¹ and even during pregnancy without any side effects.¹²

MATERIAL AND METHODS

Male Wistar rats of 8-12 weeks, weighing 200-250 grams were used for the study and they will be divided into 3 groups. Each group will be assigned 6 rats. All rats will be fed with standard diet. Group 1 was a control group and were administered with placebo i.e., distilled water. Group 2 was a toxic group and was administered with 6 mg/kg/body weight/day of Cyclophosphamide intra peritoneal for 20 days. Group 3 was also a toxic group and was administered with 6 mg/kg/body weight/day of Cyclophosphamide intra peritoneal for 20 days followed by administration of *Ashwagandha siddha Grutha* for 20 days. The dose of *Ashwagandha siddha Grutha* was 4.5 ml/kg/body weight/day.

Blood samples were collected through Orbital plexus for assessment of parameters. The assessment parameters were Haemogram, Platelet count, SGOT, SGPT, blood urea, serum creatinine.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS software version 16. The observations obtained were analyzed using one way ANOVA followed by Dun net multiple 't' test.

The data in the above table shows that there is a considerable decrease in Haemoglobin concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be

statistically significant. The test drug Ashwagandha siddha grutha showed considerable increase in haemoglobin concentration in comparison with Cyclophosphamide group.

Table 2: Effect of *Ashwagandha siddha grutha* on Total count

Group	Total count MEAN \pm SEM	% change
Control(tap water 5ml/kg)	9910 \pm 1079.0	-
Cyclophosphamide control 6mg/kg/BW	2990 \pm 411.35**	69.82 @
Ashwagandhasiddagrutha 4.5ml/kg/BW	3820 \pm 251.57	27.75 #

**P<0.01, @- Compared with normal control, #- compared with Cyclophosphamide control

The data in the above table shows that there is a considerable decrease in Total count concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statisti-

cally significant. The test drug Ashwagandha siddha grutha showed considerable increase in Total count concentration in comparison with Cyclophosphamide group.

Table 3: Effect of test drug *Ashwagandha siddha grutha* on RBC

Group	RBC MEAN \pm SEM	% change
Control(tap water 5ml/kg)	7.95 \pm 0.17	-
Cyclophosphamide control 6mg/kg/BW	7.37 \pm 0.12*	7.29 @
Ashwagandhasiddagrutha 4.5ml/kg/BW	7.54 \pm 0.12	2.30 #

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control

The data in the above table shows that there is a considerable decrease in RBC concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statisti-

cally significant. The test drug Ashwagandha siddha grutha showed considerable increase in RBC concentration in comparison with Cyclophosphamide group.

Table 4: Effect of test drug *Ashwagandha siddha grutha* on Platelet count

Group	Platelet MEAN \pm SEM	% change
Control(tap water 5ml/kg)	7.27 \pm 0.16	--
Cyclophosphamide control 6mg/kg/BW	8.68 \pm 0.72*	19.39@
Ashwagandhasiddagrutha 4.5ml/kg/BW	9.51 \pm 0.42	9.56#

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control

The data in the above table shows that there is a considerable increase in platelet concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statisti-

cally significant. The test drug Ashwagandha siddha grutha showed considerable increase in platelet concentration in comparison with Cyclophosphamide group.

Table 5: Effect of test drug *Ashwagandha siddha grutha* on SGOT

Group	SGOT MEAN \pm SEM	% change
Control(tap water 5ml/kg)	157.8 \pm 18.21	--
Cyclophosphamide control 6mg/kg/BW	129.1 \pm 3.83*	18.18@
Ashwagandhasiddagrutha 4.5ml/kg/BW	113 \pm 3.99	28.39#

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control

The data in the above table shows that there is a considerable decrease in SGOT concentration in Cyclophosphamide

administered group in comparison to normal control group and it is found to be statistically significant. The test drug Ashwa-

gandha sidda grutha showed considerable decrease in SGOT concentration in comparison with Cyclophosphamide group.

Table 6: Effect of test drug *Ashwagandha sidda grutha* on SGPT

Group	SGPT MEAN \pm SEM	% change
Control(tap water 5ml/kg)	129 \pm 23.56	--
Cyclophosphamide control 6mg/kg/BW	64.2 \pm 3.42*	50.23@
Ashwagandhasiddagrutha 4.5ml/kg/BW	61.9 \pm 3.28	3.58#

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control. The data in the above table shows that there is a considerable decrease in SGPT concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statistically significant. The test drug *Ashwagandha sidda grutha* showed considerable decrease in SGPT concentration in comparison with Cyclophosphamide group.

Table 7: Effect of test drug *Ashwagandha sidda grutha* on UREA

Group	UREA MEAN \pm SEM	% change
Control(tap water 5ml/kg)	55.7 \pm 1.74	--
Cyclophosphamide control 6mg/kg/BW	34 \pm 1.60*	38.95@
Ashwagandhasiddagrutha 4.5ml/kg/BW	21.8 \pm 1.57	35.88#

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control. The data in the above table shows that there is a considerable decrease in Urea concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statistically significant. The test drug *Ashwagandha sidda grutha* showed considerable decrease in Urea concentration in comparison with Cyclophosphamide group.

Table 8: Effect of test drug *Ashwagandha sidda grutha* on CREATININE

Group	CREATININE MEAN \pm SEM	% change
Control(tap water 5ml/kg)	0.75 \pm 0.05	--
Cyclophosphamide control 6mg/kg/BW	0.64 \pm 0.02*	14.66@
Ashwagandhasiddagrutha 4.5ml/kg/BW	0.45 \pm 0.016	29.68#

*P<0.05, @- Compared with normal control, #- compared with Cyclophosphamide control. The data in the above table shows that there is a considerable decrease in Creatinine concentration in Cyclophosphamide administered group in comparison to normal control group and it is found to be statistically significant. The test drug *Ashwagandha sidda grutha* showed considerable decrease in Creatinine concentration in comparison with Cyclophosphamide group.

DISCUSSION AND CONCLUSION

The immune system of a human being is an integral part of human protection against disease. This immune system has been shown to be suppressed in many dis-

eases and cancer in one among them. Chemotherapy and radiation therapies even though useful in management of cancer, they are found to deteriorate the immune system. Variety of materials from the plant source has been known to stimulate the haemopoietic system and act by the maturation of the immune cells.

In this modern era, there is an increase in search for a ideal drug that is capable of modifying immune system with less or no serious side effects. Scientists view the herbal drugs with interest as they are generally available in bulk quantity. Other im-

portant reason is the immune stimulatory activity of medicinal plants, less or no side effects and oral efficacy suggests that they can be used as an adjuvant in treatment of diseases like cancer. The present study was conducted with the aim of investigating immunomodulatory activities of *Ashwagandha siddha Grutha*.

The genus *Withania* is a member of family Solanaceae. *Withania somnifera* (L.) Dunal commonly known as Ashwagandha is a highly valued medicinal plant with diverse therapeutic uses in the traditional Indian systems of medicines such as Ayurveda, Unani and Siddha. Administration of *Ashwagandha siddha Grutha* was found to increase Haemoglobin, RBC, Total count and platelet concentration. It was also found in the present study that administration of *Ashwagandha siddha Grutha* significantly reduced SGOT, SGPT, Urea and Creatinine levels in Cyclophosphamide induced toxicity in Wistar rats. Thus the present study concluded that *Ashwagandha siddha Grutha* could alleviate the cell damage caused by Cyclophosphamide in Wistar rats.

REFERENCES

1. World Health Organization. The Global Burden of Disease: 2004 Update. Geneva: World Health Organization; 2008.
2. National Cancer Registry Program (ICMR), 2008
3. Nandakumar A. National Cancer Registry Programme. Indian Council for Medical Research, Consolidated report of the population based cancer registries 1990-96. New Delhi: ICMR; 2009
4. Isselbacher. Braunwald. Wilson. Martin Fauri Kasper. Harrison's Principles Of Internal Medicine, 13th edition: McGraw-Hill, Inc; 1994.p. 1834

5. Leemol Davis. Girija Kuttan. Suppressive effect of cyclophosphamide induced toxicity by *Withania somnifera* extract in mice; J. of Ethnopharmacology; 62. p. 209–214
6. <http://en.wikipedia.org/wiki/Cyclophosphamide>
7. Dorland's. Illustrated Medical Dictionary, 30th edition: Saunders an Imprint of Elsevier; 2000.p. 470-471
8. Leemol Davis. Girija Kuttan. Suppressive effect of cyclophosphamide induced toxicity by *Withania somnifera* extract in mice; J. of Ethnopharmacology; 62. p. 209–214
9. Dr Brahmanand Tripathi. Astanga Hridayam Of Sri Madhava Bhata: Chaukamba Sanskrit Pratishthan Delhi; 1999 .35th chap. p 1142
10. Dr Brahmanand Tripathi. Astanga Hridayam of Sri Madhava Bhata: Chaukamba Sanskrit Pratishthan Delhi; 1999. 5th chap. p. 73
11. Sharma k, Dandiya P.C, 1991. *Whitania somnifera* linn dunal: present status. Indian Drugs 29 (6), 247-250
12. Kuppuranjan k, rajagopalan v, janaki k, revathi r, venkataraghavan s, 1980. Effects of Ashwagandha on process of Ageing on human volunteers. J. res. Ayurveda Siddha, 247-258.

CORRESPONDING AUTHOR

Dr. Goutham S. P.
PG scholar, Dept of Agada Tantra,
S. D. M. College of Ayurveda,
Hassan, Karnataka, India
Email: dr.gouthamsp@gmail.com

Source of support: Nil

Conflict of interest: None Declared