

Griseofulvin

Aspergillus amstelodami

(2007/11/1 2007/8/15)

Aspergillus amstelodami Griseofulvin (GRF)
/ 1500 1250 1000 500

(NUV) Near UV

.
8- Azaguanine (azg)
GRF
.

Genetic Effect of the Antifungal Griseofulvin in *Aspergillus amstelodami*

Sahi J. Dhahi Hiba K. Mahmood

*Department of Biology
College of Science
Mosul University*

ABSTRACT

The present work aimed at investigating two genetic aspects of the antifungal Griseofulvin (GRF) in the ascomycetous fungus *Aspergillus amstelodami*. The first was its ability to act as a mutagen and the second was its ability to act as a photosensitizer for

the DNA to be mutated by the non-mutagenic near UV(NUV). To this end, four sublethal or subinhibitory concentrations (500, 1000, 1250, 1500 µg/ml) of the antifungal were tested for their ability to induce forward mutations resist to the toxic base analogue 8-azaguanine(*azg*) in conidia of this fungus. Within the experimental conditions specified in the present work, non of these two endpoints was fulfilled.

.(Sheppard and Lampiris, 2004)

.(Bordon – Pallier et al., 2003)

(Dermatophytes)

(Microtubules)

.(Mims et al., 2004) (Nucleic acid)

.(Knasmuller et al., 1997) (Embryotoxicity)

(Ciccone and Wolf, 1990) (Skin photosensitivity)

(Photosensitizer)

(Lee et al., 1999) (Substrate)

.(Vassileva et al., 1998)

.*Aspergillus amstelodami*

(Point mutation)

(Photosensitizer)

8-azaguanine

.(Near UV)

:

Aspergillus amstelodami (wA1)A1

(wA1)

:

.(1979) Caten

.M (Minimal medium)

(Malt Extract – Salt medium)

(D) Sodium deoxycholate

.MTS

(D) / 400

pH

.MD

M

. °30

.(6.2)

:

:Griseofulvin (GRF)

(Tablets)

Grisodin

(SDI) /

500

.(White, 1971)

10 (500)

/ 50000

: 8 – azaguanine (AZG)

Fluka

0.25

/

2500

100

(1N NaOH)

:8 – Methoxypsoralen (8–MOP)

Koch-Light

/ 1000 .Xanthotoxin
50 50
.(Igali et al., 1970)

:

:(UVA)

(NUV) (UVA) LH-335 Gallenkamp
365

:(UVC)

(UVC) NOP 189 Philip Harris (FUV)
253.7 Scottish Science

:

A1 10 .MTS

.⁰10

:(GRF) (MIC)

(Point inoculation)

A. amstelodami A1 3
M M
4 . / 2000
M M+GRF

..... Griseofulvin

.(Control)

(MIC)

.

:

/ 25

(AZG)

(⁰10)

0.1

MD + AZG

5

(⁰10)

.

0.1

MD

4-10

.3

:

×

× MD

=

. (⁰10)

.

(MD + AZG)

()

:Griseofulvin

1500 1250 1000 500

:

/

:(Pretreatment method)

-1

6

)

(

.

(Positive control)

(A1)

UVC

10 .

.UVC

. 20

10

.

:(Growth mediated method) -2

AZG

MD

MD

A1

(010)

(0)

:

MD

(UVC)

.

:(Plate incorporation method) -3

MD + (5)

(⁰10)

.

0.1

AZG

UVC

(⁰10)

.

:

(⁰10)

.

(8-MOP)

5

/

100

1

9

.(Alderson and Scott, 1970)

5

8-MOP

10

(NUV)

.....

Griseofulvin

20

(⁰10)

500

NUV

5

/

1500

1250

1000

10

:

(SE)

t(2+2)

(*t*)

Standard Error

%1

.(Steel and Torrie, 1980)

:

(MIC)

%68.38

/

250

%37.15

GRF

.

/

2000

(Sublethal)

/

1500

1250

1000

500

(1978)

Ames

McCann

DNA

(Toxic level)

:

Griseofulvin

%1

t

GRF

AZG

*t*4

4.604

t

/

1500

1250

1000

500

GRF .(1)

A. amstelodami

.MD + AZG

.(Lehne et al., 2001)

A1 8-azaguanine (6-10×) :1

Griseofulvin *A. amstelodami*

.(0)

<i>t</i>	(±) 6-10 ×				(/)
		R3	R2	R1	
	0.21 ± 0.78	0.55	0.58	1.20	0
0.33	0.22 ± 0.88	0.60	0.72	1.31	500
0.16	0.22 ± 0.83	0.42	0.93	1.15	1000
0.45	0.26 ± 0.63	0.37	0.38	1.15	1250
0.76	0.08 ± 0.61	0.52	0.54	0.76	1500
10.67**	0.88 ± 10.43	11.20	11.43	8.67	UVC

. :0

.() UVC :UVC

.%1 : **

: **Griseofulvin**

GRF

t

.(2) / 1500 1250 1000 500

A. amstelodami

.(Venitt and Parry, 1984)

..... Griseofulvin

(5) GRF :

GRF

.(Spielmann et al., 1994)

.(Aveline and Redmond, 1999)

*(In vitro)**(In vivo)*

.(Arlett et al., 1995)

A1 8-azaguanine (6-10×) : 4

A. amstelodami

.(0) Griseofulvin

<i>t</i>	(±) 6-10 ×				(GRF) (/) 8-MOP
		R3	R2	R1	
	0.03 ± 0.61	0.55	0.60	0.67	0
0.57	0.12 ± 0.54	0.39	0.78	0.45	500 GRF + NUV
1.30	0.19 ± 0.86	0.71	1.23	0.63	1000 GRF + NUV
0.50	0.18 ± 0.52	0.30	0.87	0.39	1250 GRF + NUV
0.37	0.16 ± 0.55	0.56	0.82	0.27	1500 GRF + NUV
11.70**	1.28 ± 15.59	18.09	14.80	13.88	8-MOP + NUV

. %1 : **

: GRF

.(365) 10 : NUV

.() 8- Methoxypsoralen : 8-MOP

: 0

Kassem

(2006)

(Embryotoxic)

(DeCarli and Larizza, 1988) (Organogenesis)

(Govoni et al., 1990)

Nesti

(2000)

REFERENCES

- Alderson, T. and Scott, B.R., 1970. The Photosensitising Effect of 8 – MOP on the Inactivation and Mutation of *Aspergillus* Conidia by Near Ultraviolet Light. *Mutat. Res.*, Vol. 9, pp.569-578.
- Arlett, C., Eral, L. and Ferguson, J., 1995. British Photodermatology Group Workshop: Predictive *in vitro* methods for identifying photosensitising drugs: a report. *Br. J. Dermatol.*, Vol. 132, pp.271-274.
- Aveline, B. and Redmond, R.W., 1999. Can Cellular Phototoxicity be Accurately Predicted on the Basis of Sensitizer Photophysics? *Photochem. Photobiol.*, Vol. 69, pp.306-316.
- Bordon – Pallier, F., Julian, N. and Haesslein, J., 2003. The Cell Cycle of Pathogenic Fungi: Target for Drugs. *Progress in cell cycle Research*, Vol. 5, pp.81-90.
- Caten, C.E., 1979. Genetical Determination of Conidial Colour in *Aspergillus heterocaryoticus* and Relationship of this Species to *Aspergillus amstelodami*. *Trans. Brit. Myco. Soci.*, Vol. 73, pp.65-47.
- Ciccone, C.D. and Wolf, S.L., 1990. *Pharmacology in Rehabilitation*. F.A. Davis Company. Philadelphia.
- DeCarli, L. and Larizza, L., 1988. Griseofulvin. *Mutat. Res.*, Vol. 165, pp.19-126.
- Govoni, L.A., Hayes, J.E. and David, J.A., 1990. *Drugs and Nursing Implications*. Prentice Hall, New York.
- Igali, S., Bridges, B.A., Smith, A. and Scott, B.R., 1970. Mutagenesis in *E. coli*. *Mutat. Res.*, Vol. 9, pp.21-30.
- Johnson, B.E., Walker, E.M. and Hetherington, A.M., 1986. *In vitro* Models for Cutaneous Phototoxicity. In: R. Marks and G. Plewig (eds.). *Skin Models, Models to Study Function and Disease of Skin*. Springer – Verlage, Berlin., pp.264-281.
- Kassem, M.A., Esmat, S., Bendas, E.R. and El – Komy, M.H., 2006. Efficacy of Topical Griseofulvin in Treatment of Tinea Corporis. *Mycoses*, Vol. 49, pp.232-235.

- Knasmuller, S., Parzefall, W., Helma, C., Kassie, F., Echer, S. and Schulte – Hermann, R., 1997. Toxic Effects of Griseofulvin: Disease Models, Mechanisms and Risks Assessment. *Crit. Rev. toxicol.*, Vol. 27, pp.495-537.
- Lee, A., Phil, M., Pharm, S. and Thomas, J., 1999. Drug – Induced Skin Reactions. *The Pharmaceutical Journal*, Vol. 262, pp.257-362.
- Lehne, R.A., Moore, L.A., Crosby, L.J. and Hamilton, D.B., 2001. *Pharmacology for Nursing Care*. 4th ed. W.B. Saunders Company, Philadelphia.
- McCann, J. and Ames, B.N., 1978. The *Salmonella* Microsome Mutagenicity Test: Predictive Value for Animal Carcinogenicity. In: W.G. Flamm and M.A. Mehlman (eds.). *Mutagenesis*. Hemisphere Publishing Corporation, Washington. pp.87-108.
- Mims, C., Dockrell, H.M., Goering, R.V., Riott, I., Wakelin, D. and Zuckerman, M., 2004. *Medical Microbiology*. Elsevier Mosby, London.
- Nesti, C., Trippi, F., Scarpato, R., Migliore, L. and Turchi, G., 2000. Cytokinesis – Block Micronucleus Assay in Primary Human Liver Fibroblasts Exposed to Griseofulvin and mitomycin C. *Mutagenesis*, Vol. 15, pp.143-147.
- Sandberg, S. and Romslo, I., 1981. Phototoxicity of Protoporphyrin as Related to its Subcellular Localization in Mice Liver after Short – Term Feeding with Griseofulvin. *Biochem. J.*, Vol. 198, pp.67-74.
- Sheppard, D. and Lampiris, H.W., 2004. Antifungal Agents. In: B.G. Katzung (ed.). *Basic and Clinical Pharmacology*. 9th ed. McGraw – Hill, New York. pp.792-799.
- Seif, R., 1980. Factors which Disorganize Microtubules or Microfilaments Increase the Frequency of Cell Transformation by Polyoma Virus. *J. Virol.*, Vol. 36, pp.421-428.
- Spielmann, H., Lovell, W.W., Holzle, E., Johnson, B.E., Maurer, T., Miranda, M.A., Pape, W.J.W., Sabora, O. and Sladowski, D., 1994. *In vitro* Photosensitivity Testing. *ATLA.*, Vol. 22, pp.314-348.
- Steel, R.G. and Torrie, J.H., 1980. *Principles and Procedures of Statics*. McGraw – Hill, New York.
- Suter, W. and Jaeger, I., 1982. Comparative Evaluation of Different Pairs of DNA Repair – Deficient and DNA Repair – Proficient Bacterial Tester Strains for Rapid Detection of Chemical Mutagens and Carcinogens. *Mutat. Res.*, Vol. 97, pp.1-18.
- Vassileva, S.G., Mateev, G. and Parish, L.C., 1998. Antimicrobial Photosensitivity Reactions. *Arch. Intern. Med.*, Vol. 158, pp.1993-2000.
- Venitt, S. and Parry, I.M., 1984. Background to Mutagenicity Testing. In: S. Venitt and J.M. Parry (eds.). *Mutagenicity Testing: A Practical Approach*. IRL Press, Oxford. pp.1-22.
- White, A.I., 1971. Antibiotics. In: C.O. Wilson; O. Gisvold and R.F. Doerge (eds.). *Textbook of Organic Medicinal and Pharmacological Chemistry*. 6th ed. J.B. Lippincott Company, Philadelphia., pp.343-394.