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EFFECTS OF GRISEOFULVIN ON SOME BIOCHEMICAL PARAMETERS OF WISTAR ALBINO RATS

Enoghama, O. S., Uwakwe, A.A. & Onwuka, F. C.
Department of Biochemistry University of Port Harcourt, Nigeria. P.M.B 5323, Port Harcourt, Nigeria

ABSTRACT
Griseofulvin, an antifungal agent was investigated invivo for its possible effects on some biochemical parameters of wistar albino rats (Rattus rattus). Different concentrations (0.1, 0.3. 0.7, and 1.0, all in mg/ml) of griseofulvin were administered to wistar albino rats [Rattus rattus]. The activities of the plasma enzymes, aspartate amino transferase (AST), alkaline phosphatase [ALP] and alanine amino transferase (ALT) were monitored. Total and direct bilirubin concentrations of the rats were also monitored for four weeks. The results showed an increase in AST, ALP, ALT values. Total and direct bilirubin values were observed to be high in the first week of administration, but statistically not significant P (>0.05). This increase observed were griseofulvin dosage dependent. For instance, at 1.0mg/ml griseofulvin dosage in the first week, enzymes activity and direct bilirubin values obtained were 71.5+2.1, 69.5+2.1, 66.0+1.4 and 143.0+4.2 for AST, ALP, ALT and direct bilirubin respectively, relating to their respective control values of (12.5+1.6, 21.0+1.7, 12.0+2.1 and 25.5+0.7). There were also an increase in total bilirubin (362.0+2.0) as compared to the control of (45.0+0.7)

KEY WORDS: Griseofulvin, Alkaline Phosphatase and Alanine Amino Transferase.

INTRODUCTION

Fulcin is an antifungal medication. It is like an antibiotic but is used in the treatment of fungal infections of the skins, hair and nail such as jockitch, athlete's foot and barber's itch. Its generic name is Griseofulvin which is an antifungal substance typically produced by the growth of certain strains of penicillium griseofulvum (Royal pharmaceutical society of Great Britain, 2000). A method for the synthesis of griseofulvin from dimethoxyphenol has also been reported (Pirrung *et al*., 1991). Griseofulvin is an antibiotic fungistatic drug administered orally in the treatment of dermatophyte and ringworm infections. It is fungistatic against various species of microsporum, epidermophyton and trichophyton in vitro. It is generally given for infections that involve the scalp, hair, nails, skin (example tinea corporis (ringworm of the body), tinea pedis (athelete's foot), tinea cruris (ringworm of the groin or thigh), tinea barbae (barber's itch), tinea capitis (ringworm of the scalp), tinea unguium (onychomycosis, ringworm of the nails) and which do not respond to topical treatment, infections of the soles of the feet, the palms of the hands and the nails respond slowly. (Royal pharmaceutical society of Great Britain, 2000). It is used in both humans & animals. Also, because griseofulvin has some vasodilatatory activity, its uses has resulted in some improvement in a small number of patients with Reynaud's disease and angina pectoris. Because it is structurally similar to colchicine and shares its activity as a metaphase inhibitor, griseofulvin has been used in the treatment of gout. (Royal pharmaceutical society of Great Britain, 2000).

It is fungi static; it is thought to inhibit fungal cell mitosis and nucleic acid synthesis. It also binds to and interferes with the formation of spindle and cytoplasmic microtubules by binding to alpha and beta tubulin. It does this by arresting the metaphase of cell division by disrupting the structure of the mitotic spindle. (Weber *et al.*, 1976). Also, following administration, griseofulvin is deposited in the Keratin precursor cells and becomes concentrated in the stratum corneum of the skin, hair and nail thus preventing invasion of newly formed cells by fungus.

MATERIALS AND METHOD

DRUG

Fulcin (Griseofulvin) 500mg was obtained from Reals pharmaceuticals Ltd. P.O Box 3560. Ikeja, Lagos, Nigeria.

Reagents

Aspartate Aminotransferase Kit
Alanine Aminotransferase kit
Alkaline Phosphatase kit
Bilirubin kit

ANIMAL COLLECTION/ TREATMENTS

A total of 60 Wistar Albino rats were used for the tests. These rats were obtained from the animal house of the Biochemistry department, faculty of science, University of Port Harcourt. Average weights of 100.0g -150g rats were used for the analysis. The animals where fed with their conventional diet before fulcin (griseofulvin) was introduced. This drug was administered to them by intubation. fulcin (500mg) dissolved in 500ml of distilled water was administered at different concentration of 0.1, 0.3, 0.7 and 1.0(mg/ml) to the animals which were grouped into four groups of twelve animals each to represent the four different concentrations and also there was a control group which did not get the drug. The test was monitored for a total of four weeks with three rats being sacrificed from each group every week.

RESULTS

TABLE. 1: Effect of griseofulvin (fulcin) on total bilirubin of wistar albino rats

FULCIN(mg)/ 100g Body weight	TOTAL BILIRUBIN			
	Time Interval (Weeks)			
	1	2	3	4
0.0	45.0 ± 0.7^{e}	46.7 ± 1.1^{e}	43.0 ±2.0^{e}	28.0 ± 2.0^{b}
0.1	238.0 ±2.0^{g}	71.43±3.0^{d}	49.02 ±2.7^{e}	38.7 ±1.2^{f}
0.3	279.3±3.1^{g}	81.70±1.1^{d}	53.0±1.4^{e}	39.5 ± 2.1^{f}
0.7	304.5± 2.1^{c}	86.05 ±2.0^{d}	62.9±2.4^{e}	46 0 ±2.8^{e}
1.0	362.0±2.0^{c}	98.43±3.0^{d}	70.2± 2.0^{d}	88.0± 2.5^{d}

Results are means ± SD of triplicate determinations. Values with the same superscript letters are not statistically significant at 95% confidence level.

TABLE 2: Effect of griseofulvin (fulcin) on direct bilirubin of wistar albino rats

FULCIN(mg)/ 100g Body weight	DIRECT BILIRUBIN			
	Time Interval (Weeks)			
	1	2	3	4
0.0	25.5 ± 0.7^{a}	23.65 ± 1.0^{a}	17.0 ±1.0^{b}	16.0 ± 1.7^{b}
0.1	114.3±3.1^{d}	31.3±1.5^{a}	22.3 ±2.5^{a}	18.0±1.7^{b}
0.3	117.6±1.2^{d}	36.0±2.0^{a}	23.0± 1.0^{a}	20.0±0.0^{a}
0.7	140.3±1.5^{f}	70.0±2.0^{e}	28.7±2.3^{a}	28.7±2.8^{a}
1.0	143.0±4.2^{f}	114.3±1.5^{d}	37.70± 2.5^{c}	32.0± 2.0^{a}

Results are means ± SD of triplicate determinations. Values with the same superscript letters are not statistically significant at 95% confidence level.

TABLE . 3: Effect of griseofulvin (fulcin) on aspartate transaminase of wistar albino rats

FULCIN(mg)/ 100g Body weight	ASPARTATE TRANSAMINASE			
	Time Interval (Weeks)			
	1	2	3	4
0.0	12.5 ± 1.6^{a}	11.0 ± 1.5^{a}	13.0 ±1.6^{a}	14.0 ± 1.8^{a}
0.1	47.71±1.0^{d}	13.7±1.5^{a}	15.7 ±1.5^{a}	17.7±0.6^{a}
0.3	64.0±3.5^{c}	20.5±0.5^{a}	15.3±2.1^{a}	16.0±0.0^{a}
0.7	66.7±1.5^{c}	65.0±2.0^{c}	24.7±3.1^{b}	17.5±0.7^{a}
1.0	71.5±2.1^{c}	70.3±2.9^{c}	28.0± 2.0^{b}	31.0±1.0^{b}

Results are means ± SD of triplicate determinations. Values with the same superscript letters are not statistically significant at 95% confidence level.

TABLE .4: Effect of griseofulvin (fulcin) on alkaline phosphatase of wistar albino rats

FULCIN(mg)/ 100g Body weight	ALKALINE PHOSPHATASE			
	Time Interval (Weeks)			
	1	2	3	4
0.0	21.0 ± 1.7^{a}	21.0 ± 1.7^{a}	18.0 ±1.4^{a}	16.7± 1.2^{a}
0.1	49.7±1.5^{c}	27.3±0.7^{b}	20.3 ±0.6^{a}	19.0±1.4^{a}
0.3	52.0±2.3^{d}	30.0±2.0^{b}	20.3±1.7^{a}	20.0±1.5^{a}
0.7	66.0±1.7^{d}	40.0±2.0^{c}	21.3±0.6^{a}	21.7±0.0^{a}
1.0	69.5±2.1^{d}	42.3±1.5^{c}	21.7±0.6^{a}	30.7±1.2^{b}

Results are means ± SD of triplicate determinations. Values with the same superscript letters are not statistically significant at 95% confidence level.

TABLE . 5: Effect of griseofulvin (fulcin) on alanine transaminase of wistar albino rats

FULCIN(mg)/ 100g Body weight	ALANINE TRANSAMINASE Time Interval (Weeks)			
	1	2	3	4
0.0	12.0 ± 2.1[a]	9.0 ± 2.0[a]	11.0 ±2.0[a]	13.0 ± 2.2[a]
0.1	51.0±2.0[d]	23.3±1.2[b]	14.7±1.5[a]	12.0±1.4[a]
0.3	53.0±2.3[c]	29.7±1.5[b]	16.0 ±1.7[a]	14.3±2.3[a]
0.7	60.0±2.0[c]	64.0±4.0[c]	21.0± 2.0[a]	17.0±2.8
1.0	66.0±1.4[c]	65.0±1.2[c]	26.7±3.1[b]	27.3±1.2[b]

Results are means ± SD of triplicate determinations. Values with the same superscript letters are not statistically significant at 95% confidence level.

DISCUSSION

The effect of griseofulvin (fulcin) on some biochemical parameters of wistar albino rats was assayed. Biochemical parameters investigated include total bilirubin, direct bilirubin, aspartate amino transferase, alkaline phoshatase and alanine amino transferase and results are represented in tables 1,2,3,4 and 5 respectively. The results indicated increase in the values of total bilirubin as the concentration of griseofulvin increases, with highest elevation in the first week (363.0 ± 2.0) when compared to the control value of 45.0 ± 0.7. Also the values of direct bilirubin were highest in first week of 1.0mg/ml fulcin concentration (142.0 ± 4.2) as compared to the control of 25.5 ± 0.7. The effect of griseofulvin on rat's plasma aspartate amino transferase (AST) activity as shown in table 2 indicated a progressive increase after griseofulvin administration with highest increase of 71.5 ± 2.1 at 1.0mg.ml in the first week when compared to the control of 12.5 ± 1.6. Similarly an increase in the rats' alkaline phosphatase and alanine amino transferase activities following griseofulvin administration were observed as shown in tables 4 and 5 respectively. The highest increase in rat's plasma ALP activity were obtained in the first week at 1.0mg/ml fulcin concentration while the highest increase of ALT activity were obtained in the first week at 1.0mg/ml of fulcin.

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