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INFLUENCE OF ASTIBAN ON LIVER, SPLEEN, KIDNEY AND BLADDER β.GLUCURONIDASE OF NORMAL AND *SCHISTOSOMA MANSONI* INFECTED MICE

Z. A. EL-KHOLY,* S. M. EL-ZOGHBY,* H. F. FARAG,† M. A. EL-TOUKHY,* A. A. SAAD and G. A. ABDEL-TAWAB*

*Department of Applied Medical Chemistry and
†Department of Parasitology, Medical Research Institute, Alexandria University, 22 Al-Gueish Avenue, Shatby, Alexandria, Egypt

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Abstract—This study revealed that the effect of Astiban on β-glucuronidase is not so prolonged as that observed with oxamniquine and hycanthone. Furthermore, the effect of Astiban on liver, spleen, kidney and bladder β-glucuronidase is not much greater than the effect of *Schistosoma mansoni* infection alone.

β-Glucuronidase has been implicated in the neoplastic transformation process since 1947, when Fishman [1] found that tissues from malignant neoplasms affecting different organs exhibited increased levels of the enzyme activity. Increased β-glucuronidase activity has been observed in the urine of patients suffering from urinary schistosomiasis [2–4]. *S. mansoni* infection has also been found to be accompanied by increased β-glucuronidase activity in liver, spleen and bladder tissue homogenates of infected mice [5–7]. Moreover, some antibilharzial drugs increase the activity of this enzyme. Thus, hycanthone treatment was found to be accompanied by a progressive and prolonged increase in β-glucuronidase activity when administered to normal and *S. mansoni* infected mice [5]. Recently, it has also been shown that oxamniquine increases the activity of the β-glucuronidase in the tissues of normal mice and in mice infected with *S. mansoni* [8].

The present work is aimed at studying the effect of the schistosomicidal drug Astiban (antimony dimercapto-succinate) on β-glucuronidase activity in liver, spleen, kidney and bladder homogenates of normal and *S. mansoni* infected animals.

MATERIALS AND METHODS

Swiss albino mice, 2 months old, 15 g weight, maintained on a balanced diet and kept under the same breeding conditions were used as experimental hosts. They were divided into four groups:
Group I: Normal controls.
Group II: Control mice treated with drug.
Group III: *S. mansoni* infected mice.
Group IV: Infected mice treated with drug.

Animals of Groups III and IV were infected with 100 *S. mansoni* cercarae by the paddling methods [9].

Table 1. Effect of Astiban on β-glucuronidase activity in whole tissue homogenates of liver, spleen, kidney and bladder of groups of mice with and without *S. mansoni* infection

Group	No. of mice	Mean values (± S.E.) of β-glucuronidase activity in Fishman units			
		Liver	Spleen	Kidney	Bladder
I. Controls					
a. 60 days after infection	7	1429 (101)	3028 (171)	833 (87)	871 (97)
b. 90 days after infection	9	2448 (43)	3837 (335)	1406 (170)	1140 (121)
c. 120 days after infection	8	2969 (106)	4216 (264)	1305 (90)	990 (91)
II. Normal treated					
a. 10 days after treatment	10	3354*(245)	4302*(237)	2008*(202)	1156*(86)
b. 40 days after treatment	12	3376*(265)	4377 (320)	1409 (99)	1155 (84)
c. 70 days after treatment	10	3193 (276)	4469 (358)	1849 (197)	904 (68)
III. Infected mice					
a. 60 days after infection	11	4104*(267)	5294*(413)	1624*(175)	1416*(96)
b. 90 days after infection	12	3817 (154)	5191 (331)	1536 (56)	1428 (114)
c. 120 days after infection	7	2917 (316)	4709 (179)	1462 (146)	1529 (178)
IV. Infected treated mice					
a. 10 days after treatment	11	3835*(208)	5151*(284)	1443*(93)	1252*(103)
b. 40 days after treatment	11	3701*(168)	4458 (243)	1594 (90)	1466*(40)
c. 70 days after treatment	9	3486 (241)	4201 (170)	1441 (76)	1117 (99)

* Statistically significant from the corresponding control value.

Fifty days after infection Astiban was given in five injection doses (each of 50 mg/kg) every other day to animals of groups II and IV. Mice were then sacrificed at 60, 90 and 120 days after infection. Each time, from seven to twelve mice from each group were killed and liver, spleen, kidney and bladder were quickly removed for β-glucuronidase assay. Preparation of homogenates and determination of enzyme activities were carried out as previously reported [5]. β-Glucuronidase activities were expressed in Fishman units. One Fishman unit liberates 1 μg phenolphthalein per hr at 37° [10]. Statistical analyses using the standard *t*-test [11] were made to compare the values obtained from each group with the corresponding control values. A difference with probability value of less than 0.05 was considered significant.

RESULTS

Changes in β-glucuronidase activity in the different groups are illustrated in Table 1. Ten days after treatment, β-glucuronidase significantly increased in liver, spleen, kidney and bladder homogenates of normal treated mice (Table 1, Group II), and then decreased to control levels in spleen and kidney 40 days after treatment. The significantly increased enzyme activity in liver at 40 days decreased to control level 70 days after treatment. As has been observed before [8], *S. mansoni* infection was accompanied by a significant increase in β-glucuronidase activities which decreased gradually to control levels in liver, spleen and kidney 120 days after infection.

In the *S. mansoni* infected mice (Group IV) a maximum significant increase in β-glucuronidase activities was observed in all organs 10 days after treatment with Astiban. After 40 days the enzyme activities decreased to control levels in spleen and kidney whereas it was still significantly increased in liver and bladder (3701 and 1466 units compared with 2448 and 1140 units for controls). Seventy days after treatment the enzyme activities in all organs decreased to the control values.

DISCUSSION

It is well known that β-glucuronidase enzyme increases with malignancy [12, 13]. In our present study a significant increase of β-glucuronidase activity was noted in liver, spleen and kidney 60 days after infection. This increase in enzyme activity was attributed to the biochemical and metabolic disturbances of the liver parenchyma [14]. Moreover, electron microscopic studies in murine hepatosplenic bilharziasis have shown an increase in the number of lysosomes in the parenchymal cells [15], which in turn increases the lysosomal enzyme β-glucuronidase [16, 17]. The increased β-glucuronidase activity in the liver may well be due to the intense cellular infiltrations taking place with granuloma formation 6 weeks after infection [18]. The results of this study show that Astiban treatment is accompanied by an elevation in β-glucuronidase activity and that the increasing effect of Astiban on β-glucuronidase is not so prolonged as that reported for the non-antimonial drugs oxamniquine [8] and Hycanthone [5]. Thus, β-glucuronidase activity levels reached its maximum increase 40 days after treatment and then decreased to normal levels 70 days after treatment in all the organs investigated (Table 1, Groups II and IV).

REFERENCES

1. W. Fishman and A. J. Anlyan, *J. biol. Chem.* **169**, 449 (1947).
2. G. A. Abdel-Tawab, S. M. El-Zoghby and J. M. Price, Proceedings of the First National Symposium on Bilharziasis, October (1964).
3. P. J. Fripp, *Nature, Lond.* **188**, 507 (1960).
4. P. J. Fripp, *Bull. Wld. Hlth. Org.* **34**, 423 (1966).
5. A. A. Saad, S. M. El-Zoghby, S. M. El-Sewedy, L. H. Girgis, H. F. Farag and M. Moghazy, *Biochem. Pharmac.* **27**, 473 (1978).
6. A. A. Saad, H. F. Farag, S. M. El-Zoghby, M. H. Mostafa and L. H. Girgis, *Acta Vitam. Enzym.* **31**, 179 (1977).
7. A. A. Saad, S. M. El-Zoghby, H. F. Farag, S. M. El-Sewedy, L. H. Girgis and M. Moghazy, *Acta Vitam. Enzym.* **31**, 183 (1977).
8. S. M. El-Zoghby, S. A. Ebied, Z. A. El-Kholy, A. A. Saad, G. A. Abdel-Tawab, N. A. Hammoda and Y. A. El-Gohary. In preparation.
9. G. Webbe, *Bull. Wld. Hlth. Org.* **33**, 155 (1965).
10. P. Talalay, W. H. Fishman and C. Huggins, *J. Biochem.* **166**, 757 (1946).
11. H. Arkin, R. R. Colton, *Statistical Methods*, p. 114, Barnes & Noble, New York (1963).
12. J. W. Wilkinson, in *The Principles and Practice of Diagnostic Enzymology* Ch. III, p. 154. Edward Arnold, London (1976).
13. O. C. Harold, Cirrhosis in *Diseases of the Liver* (Ed. L. Schiff) p. 867. Lippincott, Philadelphia (1975).
14. H. N. Awadalla, A. F. Sherif, A. Z. Shafei, H. A. Khalil and F. K. Girgis, *Int. J. Parasit.* **5**, 27 (1975).
15. M. A. Ramadan. *Virchows Arch. B. Zell. Path.* **9**, 1 (1971).
16. W. H. Fishman, S. S. Goldman and R. A. De Lellis. *Nature, Lond.* **213**, 457 (1967).
17. R. A. De Lellis and W. H. Fishman, *Histochem.* **13**, 4 (1968).
18. G. R. Cameron and N. C. Ganguly. *J. Path. Bact.* **87**, 217 (1964).