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<tr>
<td><strong>Author(s)</strong></td>
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<tr>
<td><strong>Citation</strong></td>
<td>日本医学放射線学会雑誌. 23(12) P.1472–P.1475</td>
</tr>
<tr>
<td><strong>Issue Date</strong></td>
<td>1964-03-25</td>
</tr>
<tr>
<td><strong>Text Version</strong></td>
<td>publisher</td>
</tr>
<tr>
<td><strong>URL</strong></td>
<td><a href="http://hdl.handle.net/11094/19083">http://hdl.handle.net/11094/19083</a></td>
</tr>
<tr>
<td><strong>DOI</strong></td>
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Osaka University
EFFECTS OF VARIOUS TYPES OF VITAMINE A AGAINST REPEATED $\gamma$-IRRADIATIONS IN MICE.

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マウスの反覆照射に対する各種ビタミンAの効果

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（昭和39年1月18日受付）

C57 BL/5 系マウス（60日令前後のもの）に，$^{60}$Co $\gamma$ 線を一回395r→週一回の照射を死亡まで続け，この間それぞれ抽出，蒸溜および，合成ビタミンAを多量に含んだ固形飼料および対照としてこれらを加えないものを，食餌として与えた。生存日数，各ビタミンA添加飼料で上記の順と逆に長くなり，その差は有意であった。この効果の相違は，各種ビタミンAの立体異性体の安定性，又は微量有効成分の相乗作用によるものではないかと考えられる。

Introduction

Restoration from radiation damage with chemical treatment has been studied in our laboratory using survival time of mice after repeated $\gamma$-irradiations as criteria. In the present investigation the effects of the supplementation of various types of vitamine A to the diet were studied in a similar way. Synthetic vitamine A, molecular distillation and solvent extraction of natural vitamine A were used for comparison. The restorative effect of natural vitamine A was demonstrated as expected from the difference in the biological effects of various types of the vitamine.

Materials and method

Mice of C57BL strain bred in the Department were used at about two months of age, average body weight 22 g. Animals were divided into four groups according to the diet supplied as shown in Table 1. Four kinds of diet in pellet form were produced by Funabashi Farms and supplied for the study. The measurement of vitamine A was carried out at Riken Vitamine Oil Co., Ltd. by its courtesy. The mice were fed the test diet from one week before irradiation and during irradiation.

Irradiations were given with $\gamma$-ray from $^{60}$Co of a therapeutic apparatus delivered at
61 r/min in air at 50 cm from the source. Whole body irradiations of 395 r were given
to every mouse once a week until death of the animal as reported previously.(1)

Changes in body weight and survival curves were compared among the four groups.
Five animals for each group were irradiated, and further five for each group were observed
as control without irradiation.

Table 1  Group of mice and composition of the diet used.

<table>
<thead>
<tr>
<th>Group</th>
<th>Diet</th>
<th>Base diet*</th>
<th>Vitamin A**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Extracted V.A diet</td>
<td>24.5 Kg</td>
<td>500 g</td>
</tr>
<tr>
<td></td>
<td>(Solvent extraction of natural vitamin A)</td>
<td></td>
<td>of extracted V.A</td>
</tr>
<tr>
<td>B</td>
<td>Distilled V.A diet</td>
<td>24.5 Kg</td>
<td>500 g</td>
</tr>
<tr>
<td></td>
<td>(Molecular distillation of natural vitamin A)</td>
<td></td>
<td>of distilled V.A</td>
</tr>
<tr>
<td>C</td>
<td>Synthetic V.A diet</td>
<td>24.5 Kg</td>
<td>500 g</td>
</tr>
<tr>
<td></td>
<td>Control diet</td>
<td>25.0 Kg</td>
<td>0</td>
</tr>
</tbody>
</table>

* As a base diet, a mixture of the same materials as those of laboratory chow produced by Fun-
  akashi Farms which contained 1% of alfalfa but omitted the addition of vitamin A and D was
  used. Only a trace of vitamin A was detected in a pellet. Of the materials fish powder contained.
  a trace of vitamin A, and the total carotin of alfalfa (a kind of pasture) was 198 p per kg which
  corresponded to vitamin A of 66.3 I. U. Each pellet contains one per cent of alfalfa.

** One gram of vitamin A had an activity of 5,000 I. U. Thus, it is expected that each mouse
  takes 500 I. U. of vitamin A when it eats 5 gr. of the diet everyday.

Fig. 1 Changes in mean body weight of animals fed with various diets.

A. Control (unirradiated)  B. Experimental (irradiated)

Changes in mean body weight of control and irradiated animals for various diets are
shown in Fig. 1 A and B: No definite difference was observed in control groups. As for
irradiated animals, the reduction of body weight was observed after fifth exposure in
control and synthetic V.A diet groups but after seventh exposure in distilled and extracted
V.A diet group.

Mean survival time and mean accumulated dose are shown in Table 2. Mean survival
times increase according to the following order: mice fed with control diet, synthetic V.A
diet and extracted V.A diet respectively. Statistically significant difference was observed
between the control diet and distilled or extracted V.A diet group as well as between
the synthetic and extracted V.A diet.

Table 2.

<table>
<thead>
<tr>
<th>Diet</th>
<th>Mean survival time (days)</th>
<th>Mean accumulated dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>29.8 ± 2.2</td>
<td>1.958 r</td>
</tr>
<tr>
<td>Synthetic V.A</td>
<td>36.8 ± 2.2</td>
<td>2.370 r</td>
</tr>
<tr>
<td>Distilled V.A</td>
<td>39.0 ± 3.3</td>
<td>2.528 r</td>
</tr>
<tr>
<td>Extracted V.A</td>
<td>51.0 ± 3.1</td>
<td>2.904 r</td>
</tr>
</tbody>
</table>

Discussion

Protective effect of vitamin A against whole body irradiation was reported by Hirakawa(1) who used liver oil as a source of vitamin A. Mortality of mice after single whole body irradiation was reported as to be reduced by the administration of the liver oil. His result was confirmed by the present study. Several hundred I.U. of vitamin A might be administered per every day in the vitamin A diet group though a few tens of I.U. in the control diet. Furthermore, it was indicated that there may be a distinct difference in the protective effect of various vitamin A samples. High bioactivity of natural vitamin A for the growth of rats that of synthetic one was reported by Baha(2). Vitamin A has two geometrical isomers, trans- and cis-type. Biologically active type of vitamin A is assumed to be trans for growth. The difference in biological efficiency may be due to the stability against isomerization of trans-type vitamin A in natural form than synthetic one though the latter contains trans-type of the vitamin more than the former(3). It is naturally assumed that, as for the stability of bioactive vitamin A, solvent extraction of natural vitamin contains more stable trans-type than molecular distillation of the same vitamin, and the latter than synthetic vitamin A. The present results are in good accordance with the above theory on the bio-potency and geometrical isomers of vitamin A. However, the possibility of contamination of highly effective component in small quantity can not be excluded.

The effect of the vitamin on survival after repeated exposures may be due to the promotion of recovery as well as the dose reduction. Any conclusion on this point cannot be reached in the present study. However, the authors have a speculation that the effect may be mainly due to the enhancement of restoration with active vitamin A. Thus, the study was carried out as one of the series of experiments on the restoration from radiation damage with chemical treatments(4).

Summary

Survival times of repeatedly irradiated mice fed the diets supplemented with various types of vitamin A were compared. Survival time increases according to the following order: control, synthetic V.A, distilled V.A and extracted V.A. The reason of the difference was discussed.

Acknowledgement

The authors wish to thank Mr. T. Tanaka for his technical assistance. They are also
greatly indebted to Riken Vitamins Oil Co. Ltd. for generous supply of the test materials and to Funatashi Farms for production of test pellets.

References