〔東京家政大学研究紀要　第32集 (2), p. 53～55, 1992〕

Effect of Fluorine on the Growing of Rats

Tomiko YOSHIHARA and Takashi AKIYAMA

(Received September 27, 1991)

Introduction

An inorganic major constituent of the animal bone or tooth consists of small crystals of hydroxy-apatite in the hexagonal crystallographic system. The actual bio-apatite has such a complicated structure as has various substituted or defective ions at each position of Ca^{2+}, PO_4^{3-}, and OH^- [1-3]. F^- is easily substituted for OH^- with shrinkage of the crystal lattice of apatite to form fluoro-apatite, resulting in hardening the structure of the bone or tooth. It is presumed that the solubility of hydroxy-apatite will gradually decrease with increase in the amount of F^- substituted. In the present study, calcium phosphate materials of various F^- contents were made from wet-process phosphoric acid containing impurities such as magnesium, iron, aluminum, fluorine, silica, and sulfulic acid, and then used for animal-feeding test.

Materials and Methods

Animals and diets. Male Sprague-Dawley strain rats (Japan Clea Co., Tokyo) weighing approximately 68—75 g were used. Animals were housed individually in wire mesh cages in an air-conditioned room (23 ± 1°C, 50—60% humidity lighted for 12 h a day (07:00 h to 19:00 h). Table 1 shows the composition of AIN-76™ mineral mixture. The composition of the experimental diet described previously[4] was based on 20% casein diet according to AIN-76™ mixture. Four kinds of calcium hydrogen phosphates such as 100% fluoro-apatite-A, 27% apatite-B, 3% apatite-C, and calcium hydrogen phosphate anhydride $CaHPO_4$ as a standard were prepared (Fig. 2). The sample A of 100% fluoro-apatite is synthesized at about 1000°C. Sample B and C were made from the defluorinated phosphoric acid obtained by adding a small amount of sodium chloride to precipitate sodium hexafluorosilicate.

Table 1. Composition of AIN-76™ mineral mixture

Ingredient	g/kg mixture
$CaHPO_4$ ★	500.0
NaCl	74.0
$K_3C_6H_5O_7 \cdot H_2O$	220.0
K_2SO_4	52.0
$MnCO_3$	3.5
$FeC_6H_5O_7 \cdot \chi H_2O$	6.0
$CuCO_3 \cdot 5H_2O$	0.3
KI	0.0078
$Na_2SeO_3 \cdot 5H_2O$	0.01
$CrK(SO_4)_2 \cdot 12H_2O$	0.55
$ZnCO_3$	1.60
MgO	24.0
Sucrose, finely powdered to make	1000.0

★ Mineral B, C or A were mixed in place of $CaHPO_4$

Animals were divided into 4 groups (5 rats per group) and fed on 4 different experimental diets contained A, B, C, D mineral mixture for 40 days. Water and diets were given *ad libitum* and their body weights were recorded daily.

Laboratory of Chemistry

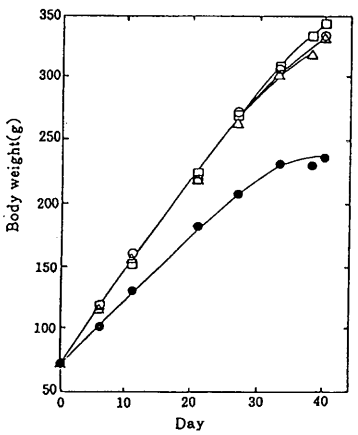

Fig. 1. Growth curves of rats

Mark	●	□	△	○
Group	A	B	C	D

Results and Discussion

As shown in Fig. 1, the body weight of group D gained at the rate of about 7 g/day. Abnormal phenomena were not recognized with the cases of group B and C as well as that of the control group D. The body weight of group A was significantly lower than the control group on day 20 and tended to decrease after the 35th day, although the bone of the rat hardened due to the crystal growth of fluoro-apatite; the rate, in addition, not only became weak but also bad alopecia after two weeks depending on the difficulty of its digestion and absorption. From these results, it is indicated that less content of apatite than 10% had no problem. On the other hand, Table 2 shows relative liver weight of rats fed A was significantly low among 4 groups; also their conditions were observed and then the liver weights were measured after feeding the mineral with various concentrations of fluorine. It was expected from these results that the human body was effected by intaking a large amount of fluorine. A great care should be taken on the food containing excessive amount of fluorine. As Umebayashi reported already that the concentration of fluorine in workers urine and serum increased with increase in the amount of

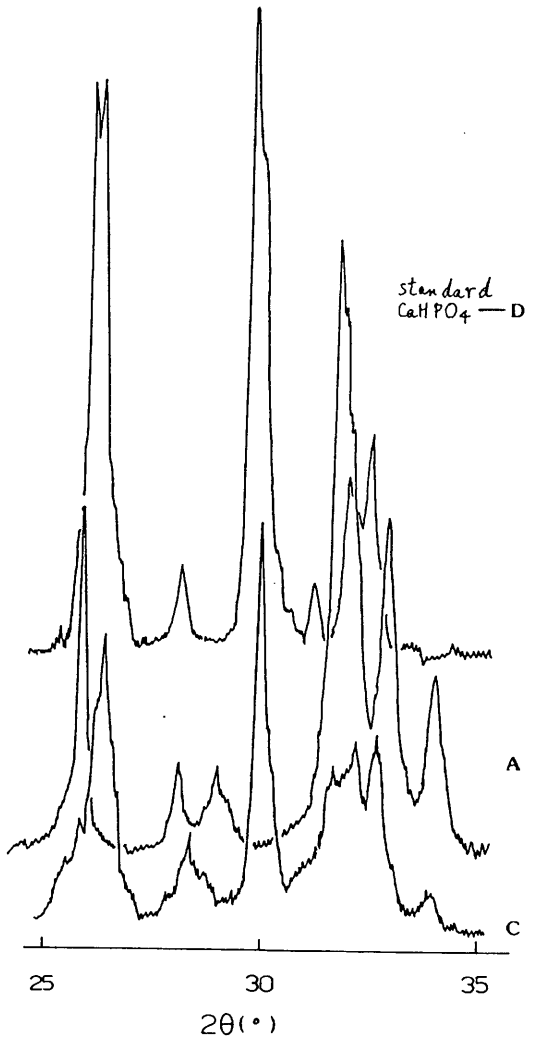

Fig. 2. X-ray powder diffraction patterns[6] of synthesized calcium phosphate (CuKα)

Table 2. Liver weight of rats (g)

Group No.	g
A	10.92±2.07**
B	16.87±3.68
C	17.47±2.57
D	15.07±1.64

Values indicate means ± SD.
Significant difference compared with group control. ** $p<0.01$

hydrochloric acid used in the fluorine chemical plant electronic industry[5], it is needed to investigate the effect of excess or deficiency of F^- on workers health. Further study will be made on the relation between the excessive amount of F^- intaked and the amount of F^- in the form of apatite used, including its influence on the function of vital defense mechanism.

References

1) Y. Itokawa: *Trace Nutrients Research* 2, 1 (1985)
2) M. Okazaki, H. Kimura, et al: *JJSMGR* 10, 7 (1991)
3) M. Saad, C. Strnad, et al: *Br. J. Pharmac.* 91, 715 (1987)
4) T. Yoshihara, Y. Hosokawa and K. Yamaguchi: *Magnesium* 8, 175 (1989)
5) K. Umebayashi, et al: *Biomed. Res. on Trace Elements* 1, 255 (1990)
6) T. Akiyama: Chemistry in Production of High-Analysis Mixed Fertilizers. Japan Research Institute for Phosphate Resources 71 (1986)

ラットの成長に及ぼすフッ素の影響

吉原富子, 秋山　堯

(平成3年9月27日受理)

食品中のフッ素は，主としてアパタイトの形態で存在しており，アパタイトの摂取が動物の成長にどのような影響を及ぼすかを調べる必要がある．今回の研究では，不純物として鉄，アルミニウム，ケイ酸，硝酸，フッ素などを含む安価な湿式リン酸を用い，これに種々の割合に水酸化カルシウムを加えて中和し，得られた沈澱物を用いてラットを飼育する試験を行った．リン酸カルシウム $Ca_3(PO_4)_2$ 3モルとフッ化カルシウム1モルの混合物を1000℃で加熱して得られた100％アパタイト食，27％アパタイト食，3％アパタイト食および標準のリン酸一水素カルシウム食の飼料をラットに40日間摂取させた．実験結果から，標準のリン酸一水素カルシウムを用いた対照群は順調に生育しており，また27％および3％アパタイト食群は対照群と非常に近い値を示した．一方，100％アパタイト食を摂取させた場合，飼育35日目から体重は，ほとんど増加せず飼育17日目頃から脱毛現象が見られた．このことから，フッ素アパタイトの結晶が成長して大きくなると溶解性が低くなり消化吸収が困難になることが考えられた．