

D)

Pentoxifylline Diltiazem

\* , \* , †

\_\_\_\_\_ :  
 \_\_\_\_\_ : Sprague-Dawley 16 , 1) , 2) , 3)  
 DIZ , 4) PIX DIZ , 4 MV 가 , 16  
 Gy . PIX 20 kg 50 mg , DIZ  
 30 kg 20 mg . 10 16 H&E  
 x<sup>2</sup>-  
 \_\_\_\_\_ : 10 PIX DIZ PIX  
 , 0.001). DIZ 가 (p value, >0.05). 16 가 10  
 가 10 가  
 \_\_\_\_\_ : PIX , PIX DIZ 가  
 PIX 가

\_\_\_\_\_ : , Pentoxifylline, Diltiazem ,

pilocarpine hydrochloride, bromhexine bethanechol chloride 가

Pentoxifylline (3, 7-dimethyl-1(5-oxyhexyl)-xanthine)( PIX )

2, 3)

4)

PIX

5, 6)

Diltiazem( DTZ )

1999 1 25 1999 7 28

apoptosis 7, 8)

9, 10)

\_\_\_\_\_ :  
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PIX DTZ

2 : Pentoxifylline Diltiazem

apop- (vacuolation) <sup>8)</sup> <sup>11)</sup>

tosis PTX DTZ 가 10 200

(vacuolation)

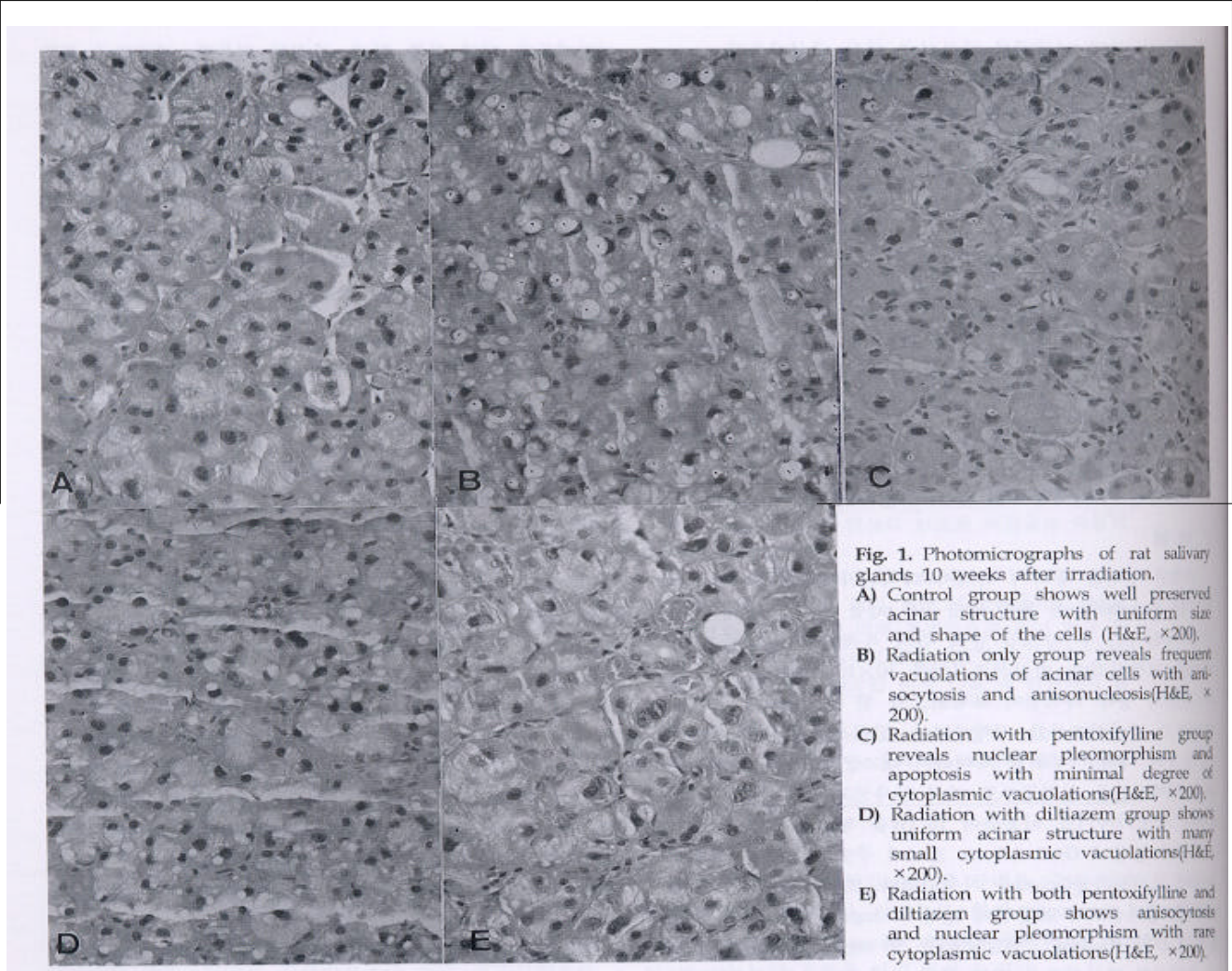
x<sup>2</sup>-test

1. 200 250g ( 8 9 ) Sprague-Dawley  
 ( ) 16 , 1) , 2)  
 PTX , 3) DTZ , 4)  
 DTZ, PTX 1. 10  
 (acinar)

2. ( , Rat )  
 (Fig. 1A).  
 ketamine kg 100 mg 가 (anisocytosis & anisonu-  
 10 × 10 cm clesis) 가 (Fig. 1B).  
 PTX apoptosis가  
 (Fig. 1C). DTZ  
 가

4 MV 가 16 Gy SSD 80 cm (Fig. 1D). PTX, DTZ  
 3 Gy 1.5 cm 5 mm (pleomorphism)  
 가 (bolus) . PTX (Trental<sup>®</sup>), (Fig. 1E).  
 ) 20 kg 50 mg  
 DTZ (Herben<sup>®</sup>, ) 50 mg 5 ml  
 30 kg 20 mg 0.448 (82.8/184.5), PTX 0.158  
<sup>8)</sup> (38.8/245.4), DTZ 0.444 (96.8/217.8),  
 10 16 DTZ, PTX 0.144 (25.4/  
 ketamine 175.6) (Table 1).  
 10% PTX ,  
 1 2 mm DTZ PTX P 0.001  
 he- DTZ P >0.05

matoxylin-eosin Masson-trichrome



**Fig. 1.** Photomicrographs of rat salivary glands 10 weeks after irradiation.  
**A)** Control group shows well preserved acinar structure with uniform size and shape of the cells (H&E, ×200).  
**B)** Radiation only group reveals frequent vacuolations of acinar cells with anisocytosis and anisonucleosis(H&E, ×200).  
**C)** Radiation with pentoxifylline group reveals nuclear pleomorphism and apoptosis with minimal degree of cytoplasmic vacuolations(H&E, ×200).  
**D)** Radiation with diltiazem group shows uniform acinar structure with many small cytoplasmic vacuolations(H&E, ×200).  
**E)** Radiation with both pentoxifylline and diltiazem group shows anisocytosis and nuclear pleomorphism with rare cytoplasmic vacuolations(H&E, ×200).

2.	16	10	
		PTX	DTZ
가	(Fig. 2A).	(Fig. 2D).	apoptotic body가
가	(multifocal)	(Fig. 2E).	
가		0.23(32.6/140),	PTX 0.123(35.8/
가		292),	DTZ 0.521 (96.2/184.5),
가		DTZ, PTX	0.144 (26.9/187.4)
가	10	(Table 1).	
가	(Fig. 2B).	PTX	PTX ,
가	(parenchymal cell)	DTZ, PTX	P 0.001
가	10	(Fig. 2C).	가
가	DTZ	DTZ	P >0.05

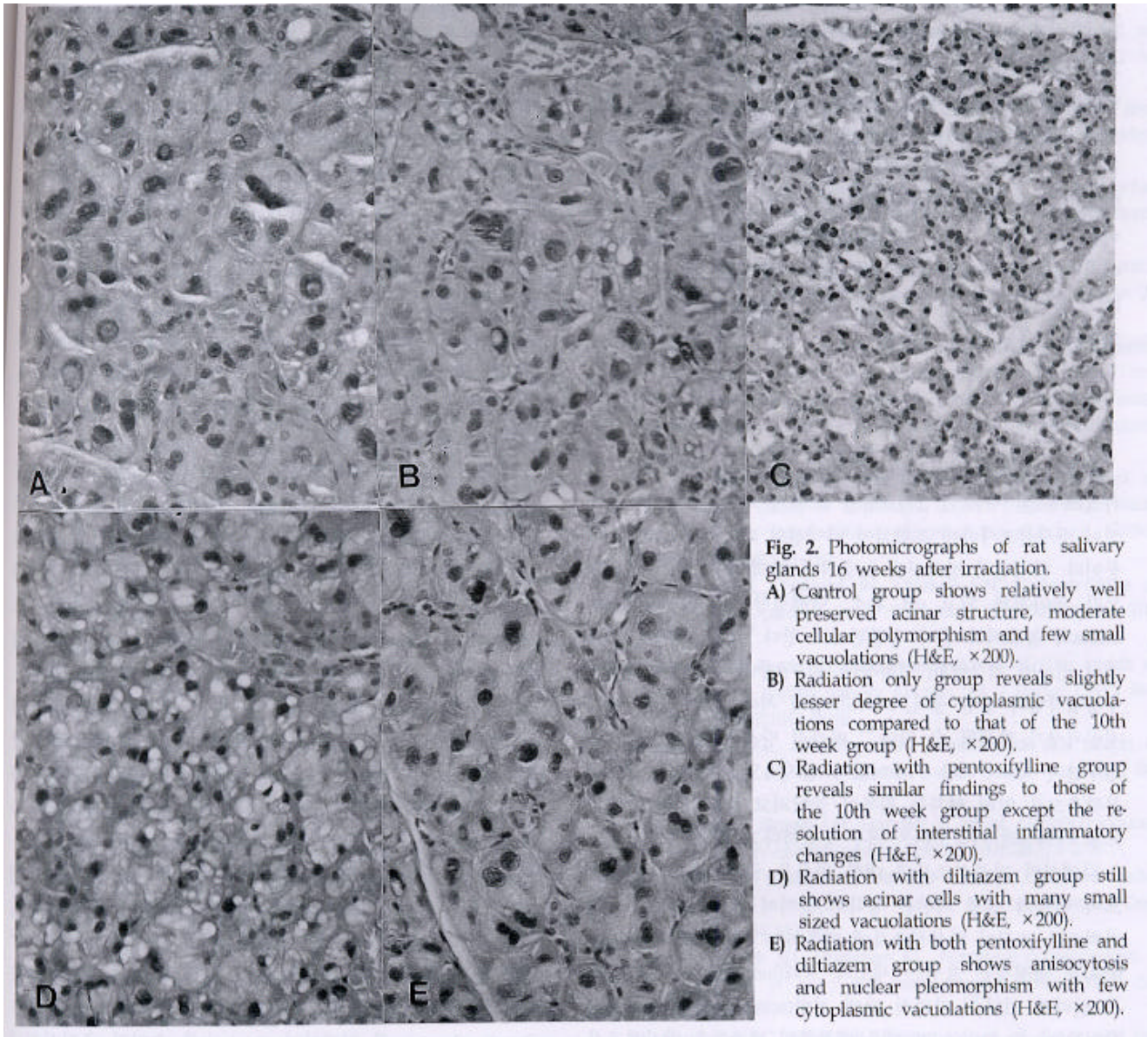


Table 1. Proportion of Vacuolated Cells of Salivary Glands among Each Experimental Groups

Post RT	10 weeks		16 weeks	
	% of vacuolated cells	<i>p</i> value	% of vacuolated cells	<i>p</i> value
RT alone	0.448 (82.8/ 184.5)		0.23 (32.6/ 140)	
RT +PTX	0.158 (38.8/ 245.4)	0.001	0.123 (35.8/ 292)	0.001
RT +DTZ	0.444 (96.8/ 217.8)	>0.05	0.521 (96.2/ 184.5)	>0.05
RT +PTX+DTZ	0.144 (25.4/ 175.6)	0.001	0.144 (26.9/ 187.4)	0.001

RT : irradiation, PTX : pentoxifylline, DTZ : diltiazem

가

가

<sup>11)</sup>

가

가

PTX

<sup>12)</sup>

PTX

ATP

cAMP

가

2, 3-DPG

가

가

<sup>28)</sup>

prostacycline

가  
bodies

pH

secretory anti-

<sup>3, 13 16)</sup>

,

<sup>17)</sup>

가

가

<sup>29)</sup>

PTX

PTX

TNF

TNF interleukin-1

(granulocyte-mediated cyto-  
cytokine

toxicity)

<sup>18 20)</sup>

(radioresponsive-

apoptosis

<sup>30)</sup>

PTX

<sup>31)</sup>

ness)

(turnover)

가

<sup>21)</sup>

(mitotic activity)가

(acini)

<sup>8)</sup>

ribose) polymerase

PTX poly (ADP-

apoptosis

<sup>32)</sup> PTX

<sup>4)</sup>

(acinar)

10 16

가

<sup>22, 23)</sup>

가 PTX

apoptosis가

PTX

가

apo-

10

apoptosis가

ptosis

<sup>24)</sup>

가 40

(interphase)

DTZ

(lethal)

<sup>23, 25, 26)</sup>

(transient)

<sup>7)</sup> DTZ

가

가

<sup>2, 19, 25)</sup>

가

<sup>33)</sup>

DTZ

<sup>27)</sup>

24 Gy

72 Gy

DTZ

<sup>9, 10)</sup>

apo-

55

ptosis

<sup>7, 8)</sup> DTZ

apoptosis

DTZ

DTZ  
 PTX,  
 PTX  
 DTZ  
 PTX  
 16 Gy  
 PTX , PTX DTZ  
 DTZ  
 가 PTX  
 subcellular level

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**Abstract**

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**Modification of Late Radiation Response of  
Rat Salivary Glands by Pentoxifylline and Diltiazem**

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**Purpose :** To elucidate the effects of pentoxifylline and diltiazem on the late response of the salivary glands of the rat after irradiation.

**Materials and Methods :** Sixteen Sprague-Dawley rats were divided into 4 groups : (a) irradiation alone (b) irradiation with pentoxifylline (PTX) (c) irradiation with diltiazem (DTZ) (d) irradiation with both PTX and DTZ. Irradiation was given in a single fraction of 16 Gy using 4 MV photon energy through an anterior port encompassing the left side of the salivary gland leaving the right side of salivary gland as a control. PTX, 20 mg/kg and/or DTZ, 50 mg/kg were infused intraperitoneally before irradiation. Two rats from each group were sacrificed on the 10th week and the rest was sacrificed on the 16th week after irradiation. Histopathologic examinations were undertaken for each section and the proportion of vacuolated cells out of the total number of cells under light microscopic fields was calculated. The statistical significance in the difference of the proportion of the vacuolated cells among the experimental groups was evaluated by a  $\chi^2$ -test.

**Results :** Irradiated salivary glands of the 10th week group revealed markedly increased number of vacuolated cells compared to those of unirradiated control. The proportion of vacuolated cells was significantly reduced in both the PTX group ( $p$  value=0.001) and the combined PTX and DTZ group compared to those of irradiation alone group. The DTZ alone group did not reveal the significant reduction of vacuolated cells compared to those of irradiation alone group ( $p$  value, >0.05). The 16th week groups revealed similar findings to those of the 10th week group, but the degree of chronic inflammatory cell infiltrates and interstitial fibrosis was increased and the number of acinar cells was reduced compared to those of the 10th week group.

**Conclusions :** PTX significantly reduced the late radiation response of salivary glands, but DTZ did not reduce the same degree as PTX did. Taking the positive results of this study into consideration, it seems reasonable to apply PTX into the clinical trial for the head and neck irradiation to reduce the late radiation sequelae of salivary glands in the near future. At the same time the further experiment to clarify the subcellular mechanisms involved in PTX should be preceded.

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**Key Words :** Salivary Glands, Pentoxifylline, Diltiazem, Irradiation, Late radiation response