

STUDY OF FIBRINOLYTIC ACTIVITY OF DERIVATIVES OF β -PHENYL- β -ALANINE AND L-TYROSINE

S.H. Kazaryan*, A.S. Aharonian*, K.P. Grigorian*

K. S. Avor**, G.P. Basmadjian**

*/*Institute of Fine Organic Chemistry RA, **College of Pharmacy, University
of Oklahoma, Health Sciences Center, Oklahoma City, Oklahoma 73190/
375014 Yerevan, 26, Azatutian Ave.*

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The problem of the mechanisms providing liquid condition of blood in the vascular channel is an important subject of scientific research. The prophylaxis and treatment of thrombosis are most updated problems of medicine [1]. The use of fibrinolytic preparations can be a promising method of thrombosis treatment.

The objective of this work is to investigate the fibrinolytic activity of four compounds – derivatives of β -phenyl- β -alanine and L-tyrosine aromatic amino acids, acting effectively on fibrinolytic system of blood.

Material and Methods

The experiments were performed on 130 rats with 120/130 *grm.* mass, 5-7 animals in each experiment series. Compounds were injected intraperitoneally at dosages of 25, 50, 100 *mg/kg* in single application in the form of 2,5% suspension of carboxymethyl cellulose and tvin.

As a biological effect analogue fibrinolysin was chosen. Its effect was studied both in experiments and in a clinic for treatment of patients with thromboembolic disease. Fibrinolysin was injected at a 1500 *un/kg* dosage intraperitoneally in a single application. Control animals were injected with the indicated suspension at the same volume.

Fibrinolytic activity and fibrinogen concentration were determined 50 minutes after the injection of the compounds, and 10 minutes after the fibrinolysin injection.

The fibrinogen concentration was determined by the Ruthberg method [2] and the fibrinolytic activity was determined by the Tulchinsky method [3]. The methods are based on the determination of fibrinolysin degree before and 24 hours after an incubation in thermostate by gravimetric method.

The acute toxicity was calculated by the Berence method on white mice with 18-20 *grm.* mass using peroral application. The data were analysed statistically using Student's criterion [4].

Results and Discussion

As the table shows, compounds 1,2, 3 at a 100 mg/kg dosage possess fibrinolytic activity, in compound 4 fibrinolytic activity is expressed poorly. *tert*-Butyloxycarbonyl-p-methoxy- β -phenyl- β -alanine (comp. 2) increases fibrinolytic activity in 45%, β -p-methoxyphenyl- β -alanine (comp. 1) and O-methoxy-L-tyrosine (comp. 3) increase fibrinolytic activity in 36% and 40%, respectively.

Table

The effect of the tested compounds and fibrinolysin on fibrinolytic activity and fibrinogen concentration

№	Compounds	Fibrinolytic activity, (%)	Concentration of fibrinogen, (mg %)
	Control	11,0 \pm 1,0	159 \pm 6,0
1.	β -p-Methoxyphenyl- β -alanine	14,9 \pm 0,4*	140 \pm 5,7
2.	<i>tert</i> -Butyloxycarbonyl-p-methoxy- β -phenyl- β -alanine	16,0 \pm 1,0*	125 \pm 7,0*
3.	O-Methoxy-L-tyrosine	15,4 \pm 0,6*	131 \pm 4,0*
4.	<i>tert</i> -Butyloxycarbonyl-O-methoxy-L-tyrosine	13,0 \pm 0,5	145 \pm 6,1
5.	Fibrinolysin	14,3 \pm 0,2*	137 \pm 3,0*

* – a reliable effect as compared with the control: $p < 0,05$.

The acute toxicity study revealed that LD₅₀ varies from 450 mg/kg to 590 mg/kg (comp. 1=550 \pm 20, comp. 2=590 \pm 15, comp. 3=480 \pm 30, comp. 4=450 \pm 20).

Thus, the results of the research prove that the derivatives of β -phenyl- β -alanine and L-tyrosine aromatic amino acids possess fibrinolytic activity providing opportunity to use this line in searching new biologically active compounds.

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Ս.Հ. Դազարյան, Ա.Ս. Մհարոնյան, Կ.Պ. Գրիգորյան,
Կ.Ս. Ավոր, Գ.Ֆ. Բասմաջյան

Ուսումնասիրվել է արոմատիկ ամինաթթուների՝ β -ֆենիլ- β -ալանինի և L-թիրոզինի ածանցյալների ֆիբրինոլիտիկ ակտիվությունը: Կատարված ուսումնասիրությունները ցույց են տվել, որ *պրեկուրսոր*ի օքսիկարբոնիլ-պարա-մեթօքսի- β -ֆենիլ- β -ալանինը (միաց.2), օժտված է ֆիբրինոլիտիկ ակտիվությամբ՝ մեծացնելով այն 45%, -ով, պարա-մեթօքսի- β -ֆենիլ- β -ալանինը (միաց.1) և O-մեթօքսի-L-թիրոզինը (միաց.3) մեծացնում են ֆիբրինոլիտիկ ակտիվությունը համապատասխանորեն 36% և 40%, իսկ *պրեկուրսոր*ի օքսիկարբոնիլ-O-մեթօքսի-L-թիրոզինը ցուցաբերում է թույլ արտահայտված ֆիբրինոլիտիկ ակտիվություն (միաց.4):

ИЗУЧЕНИЕ ФИБРИНОЛИТИЧЕСКОЙ АКТИВНОСТИ ПРОИЗВОДНЫХ β-ФЕНИЛ-β-АЛАНИНА И L-ТИРОЗИНА

С.А.Казарян, А.С.Агаронян, К.П.Григорян, К.С.Авор, Г.Ф.Басмаджян

Было исследовано фибринолитическое действие четырех соединений, являющихся производными ароматических аминокислот β-фенил-β-аланина и L-тирозина. Проведенные исследования показали, что трет-бутилоксикарбонил-п-метокси-β-фенил-β-аланин (соед. 2) повышает фибринолитическую активность на 45%, а β-п-метоксифенил-β-аланин (соед.1) и О-метокси-L-тирозин (соед. 3) повышают фибринолитическую активность соответственно на 36 и 40%; трет-бутилоксикарбонил-О-метокси-L-тирозин проявляет слабо выраженную фибринолитическую активность.

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