15. *Shipolini R. A., Callewaert G. L., Cottrell R. C., Doonan S. Vernon C. A., Banks B. E. C.* J. Biochem. 20, 459, 1971.
16. *Tanaka Y., Eriomin V. A., Kawamura Y., Inou K., Najima S.* J. Biochem., 94, 3, 841—846, 1983.
17. *Teramoto T., Toji H., Yamano T., Okamoto M.* J. Biochemistry, 93, 5, 1353—1361, 1983.
18. *Weber K., Osborn M.* J. Biol. Chem., 244, 16, 4406—4412, 1969.
19. *Wells M. A., Hanahan D. J.* Methods in Enzimol., 14, 179—181, Acad. Press., New York—London, 1969.

Поступила 25.II 1985 г.

Биолог. ж. Армении, т. 40, № 6, 358—364, 1987 УДК 577.15:579.22+579.6

ENZYMATIC CHARACTERIZATION OF A NEW HYDROLASE FROM MICROBIAL ORIGIN

BOHOS KEVORK AESROB AND STANKA PETCOVA STOEVA
Dept. of Organic Chemistry, Inst. of Chemical Technology Sofia, Bulgaria

Abstract — The enzymatic properties of proteolytic enzyme isolated from *Bac. mesentericus* strain 76, selected by bulgarian microbiologists were investigated. The proteinase named as "MCP 76" (milk-clotting proteinase) is a metaloenzyme of 33000 mol. weight.

On the basis of the enzyme properties and structure the new enzyme is considered a metal-chelator-sensible alcaline proteinase, which is too strange to find its place in the Morihara classification, but can be defined after Dixon and Webb as 3.4.2.1. *Bac. mesentericus* alcaline proteinase.

Аннотация—Изучены ферментативные свойства протеолитического фермента, изолированного из *Bac. mesentericus* (штамм 76)—болгарскими микробиологами. Молокосвёртывающая протеиназа, названная «MCP 76» является металоэнзимом с м. в.—33 000.

На основе изучения свойств и структуры нового фермента он определен как чувствительный к хелатам металлов алкалин-протеиназа, которая слишком необычна, чтобы классифицироваться по системе Морихары, но может быть определена по Диксону и Уэбб как 3.4.2.1.1. Bac. mesentericus alcaline proteinase.

Անոտացիա — Ուսումնասիրվել են Bac. mesentericus (շտամ 76)-ից, բնորոշված բուլղարական միկրոբիոլոգների կողմից, անչուռված պրոտեոլիտիկ ֆերմենտի ֆերմենտատիվ հատկություններն։ Կաթ թանձրացնող պրոտեինազը, որն անվանված է «MCP 76», 33000 մոլ. կշռով մետալոֆերմենտ է։

Ֆերմենտի հատկությունների և կառուցվածքի ուսումնասիրման հիման վրա նոր ֆերմենտը համարվել է մետաղների խելատների նկատմամբ զգայուն ալկալային պրոտեինազ, որը չափից դուրս արտասովոր է, որպեսզի պատկարգվի բատ Մորիհարայի սիստեմի, բայց կարող է բնորոշվել բատ Դիքսոնի և Ուեբբի որպես 3.1.24.4. Bac. mesentericus alcaline proteinase.

Key words: milk-curdling enzyme, alcaline protease, Bacillus mesentericus.

The hydrolase, subject of our report is a proteolytic enzyme isolated from *Bac. mesentericus* strain 76, selected from bulgarian microbiologists [1]. Once established as an industrially interesting enzyme, they were elaborated new growth conditions of this strain, getting higher en-

zyme productivity [2]. This proteinase, named from us „MCP 76" (milk-clotting proteinase from strain 76), having an alcaline optimum (pH 9,0) of peptidase activity [3] one Zn-atom per molecule in native state [4,5], stabilised by unidentified number of Ca-atoms [6], is isolated from the extracellular liquor and prepared in chemical pure state by ethanol-precipitation and anionexchange column chromatography [7]. MCP76 is a metaloenzyme of 33300 mol. weight, single polypeptide chain with 301 amino acid residues, missing cystins [5]. With its N-terminal arginine and masked C-terminus it is histidine protein [8]. Beside the typically endopeptidase activity the enzyme demonstrates an esterase activity and high milk-clotting possibility. So it became a very good microbial rennin-substituent for the cheese making industry. By its amino acid composition, sensibility to specific amino acid-modifying reagents, as well as by some enzymatic properties MCP 76 resembles the thermolysine from *Buc. thermoproteolyticus* [9]. Its individuality is established by the sequence of 15 amino acid residues from the N-terminus [10], which differs from all the Zn-proteases with known amino acid sequence and from thermolysin too [11, 12].

The aim of this proceeding is to discuss the enzymatic properties of MCP 76 in connection with its usefulness in other fields of specific hydrolysis, in the enzyme catalysed peptide synthesis and so on.

Proteolytic and esterolytic activity of MCP 76. The proteolytic activity was determined towards high molecular weights substrates: 2% Hammarsten casein solution in 0,1 M KCl + mM $CaCl_2$ and 2% solution of urea-denatured hemoglobin [13, 15]. For the esterase activity were used the following substrates: BAEE, TAME, ATEE, TEE BTME*. The enzyme catalysed hydrolysis of the substrates was followed using Radiometer autotitrator with pH state and after the absorption changes of the substrate solutions: for BAEE at 253 nm; for TAME at 247 nm; for ATEE and TEE at 237 nm and for BTME at 256 nm [16, 17].

The pH-activity curves for the hydrolysis of casein and urea denatured hemoglobin by the action of the MCP 76 showed an optimum pH at 8.5—9.0 for the hydrolysis of casein and pH 8.5—9.2—for hemoglobin. There is a difference in the pH-activity-pH curves for both substrates in the pH region 6.3—6.9, where case in hydrolysis is about 1.5—times greater than hemoglobin hydrolysis under the same conditions. The activity of MCP 76 on synthetic substrates showed an optimal pH 6.6 for the hydrolysis of TEE and pH 8.0 for the hydrolysis of BAEE. The rate of the TEE—hydrolysis is 4-times higher than of BAEE under the same conditions. The K_m for TEE and BAEE—hydrolysis determined at the optimal pH for each substrate is 83 mM for TEE and 26.6 mM for BAEE (Fig. 1).

The esterase activity of MCP 76 towards the other esters was tested comparatively with DFP—treated—MCP 76, trypsin and chymotrypsin. Each enzyme was investigated at its pH—optimum. It was established

---

* Abbreviations: BAEE—N—α—benzoyl—L—argininеethylester; TAME—N—α—tosyl—L—argininemetaylester; ATEE—N—acetyl—L—tyrosineethylester; TEE—L—tyrosineethylester; BTME—N—benzoyl—L—tyrosinemethylester.

that the trypsinlike and chymotrypsinlike esterase activity of MCP 76 is about 10—times weaker than that of active trypsin and chymotrypsin [15]. The drop in activity after DFP—treatment is 3—5% vs. both typical trypsin and typical chymotrypsin substrates only after 4—hours of incu-

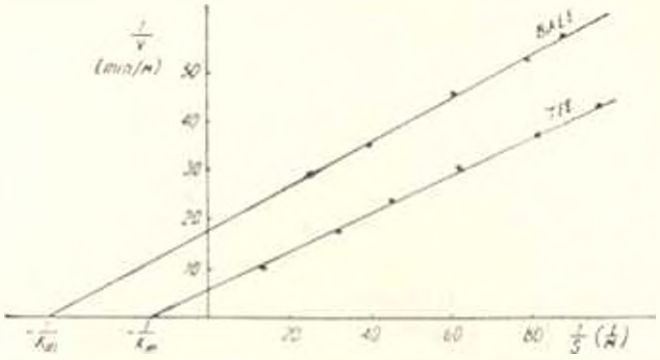

Fig. 1. K_m — values for the hydrolysis of TFE and BAEE by the action of MCP76.

bation. Consequently, from the results obtained it may be assumed, that the MCP 76 esterase activity towards specific tyrosine and chymotrypsin substrates is its own property and is not due to serine—protein contamination. On the other hand, the slow and weak effect of DFP on MCP 76 may be ascribed to possible nonspecific interactions with serine residues out of the active site, leading to a violation of the enzyme native conformation. The pH—optimum of 8.5—9.0 is a typical alcaline proteinase property, but the lower proteolytic activity of MCP 76 at pH 5.8—6.0 makes it suitable as cheese making enzyme.

The potential usefulness of MCP 76 as a microbial rennin-substituent was the reason of our investigation on its phosphoesterase activity. Phosphomonoesterase activity was determined at pH 6.5 and 9.0 after the released p—nitrophenol from p—nitrophenylphosphate as a substrate [18]. For the phosphodiesterase activity bis—(p—nitrophenyl)—phosphate as a substrate was used [19]. The absorbance at 400 nm was measured and the activity was calculated on the basis of molar absorption coefficient $17 \times 10^3\ M^{-1}\ cm^{-1}$ of the released by the enzyme action p—nitrophenol.

The experiments show the predominance of phosphodiesterase activity at pH 6.5 of higher velocity than at pH 9.0 [20].

The established esterase activity of MCP 76 is not surprising. Some neutral Zn—proteases from *Bac. thermoproteolyticus*, *Bac. subtilis* and *Aeromonas proteolytica* hydrolyse ester binding too [21]. This fact implies that esterase activity is a property of Zn—proteases at all. The presence both of proteolytic and esterase activity in MCP 76 indicates according to Holmquist and Vallee [21] that ester and peptide bond hydrolysis proceeds by identical binding and catalytic mechanism.

As a proteinase, MCP 76 has a high hydrolytic capacity towards casein. Studying its proteolytic activity after the release of TCA—soluble nitrogen, MCP 76 showed about 5 and 2.5—times higher activity than

the rennin and the pepsin respectively, by the same conditions. By the kinetic study of this reaction at pH 6.5 was established, that rennin and pepsin catalysed reaction ended after about 10 min, while MCP 76 hydrolysed even after 60 min still by the same initial velocity. This contradiction in the hydrolysis rates obtained we explain with the phosphoesterase activity of the enzyme, leading to the split both of peptide and phosphoester bonds of casein fractions. This fact was confirmed with the drastic change of the electric charges of MCP 76—treated casein fractions, established by PAGDE.

The MCP 76—catalysed hydrolysis reaction specifity was studied on oxydized insulin B—chain. After fractionation of the peptides obtained and determination of the sites and rates of splitting, the specifity of MCP 76 was demonstrated in comparison with known metal—chelator—sensible neutral and alcaline proteases, as well as with rennin and some rennin—substitutes (Fig. 2) [20].

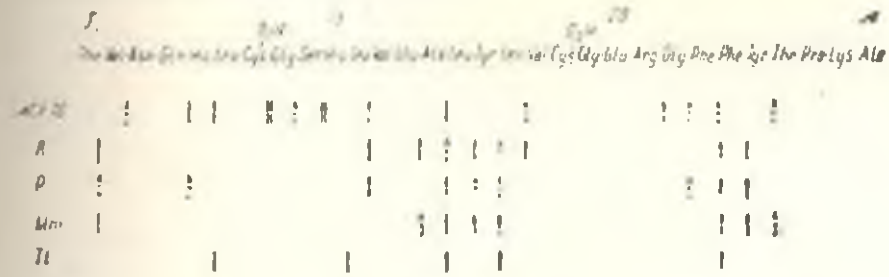

Fig. 2. Site of cleavage of oxydized insulin B - chain by MCP76 and other proteases. R — calf rennin, P — bovin pepsin, Mm — bacterial protease from Mucror miehei (milk-clotting enzyme), Tl — thermolysine.

Our results, obtained by using of low and high—molecular peptide substrates indicate (Fig. 2), that MCP 76 hydrolyses mainly peptide bonds, containing amino groups of hydrophobic amino acids of glycine and histidine.

This type of specificity is characteristic of the neutral metal—chelator—sensible proteases. They split mainly peptide bonds containing amino group of leucine, valine, phenylalanine and tyrosine. There are only small differences between the specifity of MCP 76 and these proteases. But MCP 76 differs significantly from the alcaline metal—chelator—sensible proteases (according the classification of Morihara [22]). The hydrolysis activity of these proteases is of lower specifity—they split from both the amino and carboxy side of same amino acids.

As can be seen (Fig. 2) the enzyme splits at different rates the same bonds in different surrounding in the B—chain (bonds Cys—Gly at 7—8 and 19—20). This result supports the hypothesis on the more complicated structure of the MCP 76 catalytic centre—the presence of secondary contact sites necessary in the binding of the substrate molecule, like the structure of pepsin [23] and some other peoteases. In this case the hydrolysis rates depend on the neighbouring residues around the sensitive peptide bond.

We studied the MCP 76—catalysed reaction small peptide substrates too. The enzyme was practically inactive towards nonprotected dipeptides at pH 6.5. The reaction was carried out on the peptide chosen:

1) Z—L—Tyr — L — Ile — OH; 2) Z —L — Thr — L — Phe — OMe;
3) Z— L—Pro — L — Leu — GlyOH; 4) Z—L—Phe—L—Met—OH;
5) Furoyl—acryloyl—Gly—L—Leu—ONH_2 (FAGLA).

The reasons for this choice were: the first three contain MCP 76——accessible peptide bonds; No 4—the presence of Phe—Metbond—a—casein bond mainly splitted from rennin in the milk—clotting process [24] and FAGLA—a specific thermolysin substrate [25]. The hydrolysed bond in each peptide was estimated by TLC of the obtained fragments. The peptides 1—4 were dissolved in 12.5% aceton in buffer (pH 6.5 and 9.0). The results are given in Table 1.

Table 1 Rate and specifity of MCP 76—catalysed hydrolysis of protected peptides

Substrate (in 12.5% aceton in 50 mM KCl +1 mM $CaCl_2$	Hydrolysis rate (u l 10 mM KOH/min)		Hydrolysis fragments* (TLC solvent systems)**	
	pH 6.5	pH 9.0	S 1 and S 2	S 3
Z—L—Tyr—L—Ile—OH	3.0	3.0	Z—Tyr	Ile—OH
Z—L—Thr—L—Phe—OMe	1.0	3.0	Z—Thr, Phe—OMe Z—Thr—Phe—OH	Phe—OH
Z—L—Pro—L—Leu—Gly—OH	0.3	0.7	Z—Pro, Z—Pro— —Leu	Gly—OH, Leu—OH
Z—L—Phe—L—Met—OH	10.0	0.5	Z—Phe	Met—OH

* By TLC on Silufol plates.

** S1 — Chloroform, acetic acid (9:1) (for protected peptides, Reindle detection

S2 — n — Butanol : water : pyridine : acetic acid (60:20:24:6) (for protected peptides, Reindle detection)

S3 — n — Butanol : acetic acid : water : pyridine (15:3:12:10) (for free amino acids, ninhydrin detection).

The resulting specificity of MCP 76 is as follows:

Z—Tyr—Ile—OH; Z—Thr—Phe—OMe; Z—Pro—Leu—Gly—OH;
Z—Phe—Met—OH.

By the peptides studied there is no split of Z—Y bond (Y=Tyr, Thr, Pro, Phe). The comparatively higher rate of Phe—Met—bond hydrolysis by MCP 76 makes this enzyme effective as rennin—substitute.

The pH—optimum of the MCP 76—catalysed hydrolysis of Z——Phe—MetOH was determined in study of titration curves. The titrations with 19mM KOH were carried out using an autotitrator—pH—stat, on 1 ml portions of 100 mM substrate solution in 50% DMSO in 10 mMKCL + 5mM $CaCl_2$, with 5 Mg MCP 76 (~0.15 M moles) in 30 ML 100mM acetate buffer pH 6.5. The results (Fig. 3) show a sharp pH—optimum of about pH 5.1.

The peptidolytic activity of MCP 76 towards FAGLA was estimated by the drop of the absorption at 345 nm [25]. The pH—optimum was deduced by using of 1mM FAGLA solutions in buffers of different pH. In Fig. 4 is plotted the pH 6.5 as optimum.

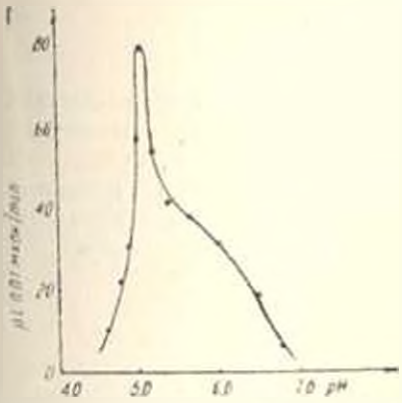

Fig. 3. pH — dependence of the hydrolysis velocity of Z–Phe—Met—OH as substrate by MCP76.

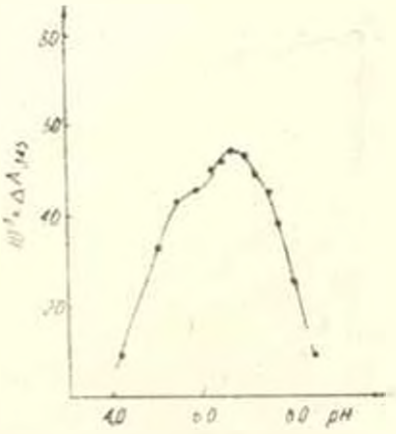

Fig. 4. pH — dependence of FAGLA cleavage by MCP76.

It can be seen, that MCP 76 shows an activity towards ester and peptide bonds in synthetic esters and low—and high—molecular peptides and proteins at different pH (between 5.1—9.2) dependent from the substrate and the type of the solvent media (water, water—organic solvents or water Luis acids). This is in accordance and supports the idea of easier adaptation of microbial proteinases towards different substrates. It is supported by potentiometric titration of MCP 76, when occur significant conformational changes in the enzyme structure 26. These changes became deeper, when to the influence of pH is added the possible solvation of more hydrophobic areas of enzyme molecule by organic solvents. In these conditions the adaptation of the enzyme reactive centre structure to the different substrates seems to be a favorable process.

Inhibitory effects on MCP 76. The search of an effective inhibitor of MCP 76 had two reasons: if the trypsinlike or chymotrypsinlike esterase activity or the proteolytic are not due to other enzyme contaminations of serine type. On the other hand—to eliminate the autolysis of enzyme preparations during the investigation.

The following specific polypeptide inhibitors were tested: bull sperm—plasma—inhibitors (BUSI I and BUSI II), „Contrical" (CIDR)—a formulation of trypsin—, plasmin—and kallgenase—inhibitors, ovomucoid, melittin, soya been trypsin—inhibitor. The results show lower than 6% of proteolytic activity decrease of MCP 76 treated with these inhibitors [15], demonstrating again that MCP 76 is not a serine proteinase. This low degree of inhibition may be due to the inhibitors' nonspecific interaction with MCP 76.

Chemical modification effect on the enzymatic properties of MCP 76. This study refers to the interaction of some specific amino

acid reactants, which modify mainly the specific amino acid function in the active centrum of enzymes. On the Fig. 5 are given the curves of inhibitory effect on MCP 76. From the results obtained may be summarised:

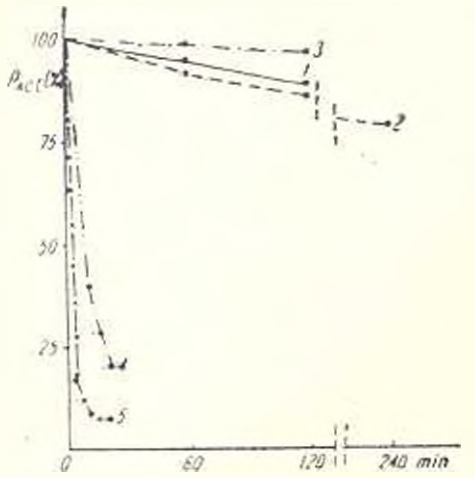

Fig. 5. Influence of specific chemical modifiers of amino acids on the proteolytic activity of MCP76: 1 — TNM (25:1)); 2 — DFP; 3 — 1, 2 — cyclohexadion (60:1) at pH 8.0; 4 — DEPC. 5 — DFP — trypsin.

The interaction of 1,2—cyclohexadion at pH 8.0, 35° [27] with MCP 76 leads to decrease of the proteolytic activity only with 3%;

The influence of DFP is nonspecific too. Only after 4—hour—treatment the loss of activity achieves 20%. In comparative study, the inactivation of trypsin occurs in few minutes [28];

Inactivation pattern of TNM (trinitromethane)—treated MCP 76 is almost the same. About 30% inactivation is observed after 2 hours and in 100—times molar excess of TNM [29].

This kind of slow and weak inactivation of MCP 76 may be due to the binding of the reagents with arginine residues (1,2—cyclohexadion), serine (DFP) or tyrosine residues (TNM) out of the catalytic centrum of the enzyme.

The interaction of diethylpyrocarbonate (DEPC) leads to drastic decrease of MCP 76 proteolytic activity [30]. This result shows a bound histidine in the reactive centrum of the enzyme. The presence of 2 accessible histidine residues on the surface of the native MCP 76 molecule was confirmed by potentiometric titration study of the enzyme [26].

Metal—chelator—effect on the MCP 76 enzymatic properties. As a Zn—proteinase MCP 76 is sensible to metal—chelators. Our investigation confirmed, that by longtime treatment with 1mM EDTA or OP (o—phtalylaldehyde) MCP 76 was irreversibly inactivated. The reversibility of this process was possible at reduced metal—chelator—treating time and at higher concentration of Ca—ions. The time—effect is shown in the Table 2.

From these results is to be seen, that the reactivation is still possible by 1 mM Ca—ions in the reaction media, if the enzyme was first treated with metal—chelator not longer than 10 min.

Table 2 Kinetic of the loss and restoration of proteolytic activity of MCP 76 at pH 6.5

Loss of activity (in 1 mM EDTA+1mM $CaCl_2$)		Restored activity (in 1mM $ZnSO_4$+1mM $CaCl_2$)		
Time min	Residual activity %	Time, min		
		5	5	13
5	23.5	36.4	32.8	34.5
10	4.5	10.9	11.2	9.6
15	1.6	—	—	—

After 10 min treating in 1 mM EDTA by 10.0 mM $CaCl_2$ at pH 6.5 and about 80% of enzymes' proteolytic activity, 100% reactivation is achieved by incubation of the apoenzyme obtained in 1 mM $ZnSO_4$ and mM $CaCl_2$ solution.

By these results was demonstrated the importance of Ca—ions for the stability of the MCP 76 native structure, established by other methods from us [6]. Probably, the irreversibility of the enzymes' inactivation by longtime treatment with EDTA or OP at low Ca—ions concentration is due to the changes in the conformation of the enzyme, insufficiently protected for lack of Ca—ions.

On the basis of the discussed enzyme properties and structure data we consider this new enzyme—the MCP 76, as a metal—chelator—sensible alcaline proteinase, which is too strange to find its place in the Morihara classification [22].

After the Dixon and Webb „Nomenclature of enzymes", must be defined as *3. 4. 24. 4. Bac. mesentericus* alcaline proteinase regarding, that the enzyme is a hydrolase (3-), which hydrolyses peptide bonds (3. *4.*), metal ion is participating in the catalytic mechanism (3. 4. *24.*) and is from microbial origin (3. 4. 24. *4'.*).

References

1. *Emanuiloff I.* Bull. Inst. Microbiol. Bulg. Acad. Sci., *2*, 1—17, 1951.
2. *Kondratenko M., Nachev L., Dedova P., Antonova T.* USPat. 4048339, 1977.
3. *Mesrob B. K., Ivanov Ch., Vassileva R. A.* Compt. rend. Acad. bulg. sci., *29*, 1349—52, 1976.
4. *Mesrob B. K., Vassileva R. A.* Int. J. Pept. Protein Res., *17*, 89—92, 1981.
5. *Mesrob B. K., Stoeva S. P.* Int. J. Pept. Protein Res., *21*, 369—373, 1983.
6. *Mesrob B. K., Stoeva S. P., Vassileva V. M.* Compt. rend. Acad. bulg. sci., *35*, 1523—26, 1982.
7. *Mesrob B. K., Stoeva S. P., Vassileva R. A.* Int. J. Pept. Protein Res., *11*, 340—344, 1978.
8. *Mesrob B. K., Stoeva S. P.* Unpublished data.
9. *Titani K., Hermodson M., Ericsson L., Walsh K., Neurath H.* Nature, New Biology, *238*, 35—37, 1972.
10. *Vassileva R. A., Mesrob B. K., Mancheva I. N.* Compt. rend. Acad. bulg. sci., *35*, 1527—30, 1982.
11. *Backer W. C., Dayhoff M. O.* In: Atlas of Protein Sequence and Structure, ed. M. O. Dayhoff, Nat. Biomed. Res. Found, *5*, 101, Washington, D. C., 1972.
12. *Lipscomb W. N., Hartsuck J. A., Reeke G. N. Jr., Quiocho F. A., Bethge P. H., Ludwig M. L., Steitz T. A., Muir—head H., Coppola J. C.* Brookhaven Symp., *21*, 24—32, 1969.

13. *Stoeva S. P., Mesrob B. K.* FEBS Letters, *90*, 1, 86–88, 1977.
14. *Anson M. L. J.* Gen. Physiol., 22, 79–86, 1938.
15. *Mesrob B. K., Stoeva S. P., Mahdi R.* Compt. rend. Acad. bulg. sci., *35*, 5 653—656, 1982.
16. *Hummel B. C. W.* Canad. J. Biochem. Physiol., *37*, 1493–95, 1959.
17. *Schwert G. W., Takenaka Y.* Biophys. Biochim. Acta, *16*, 570—578, 1955.
18. *Bessey O. A., Lowry O. H., Brock M. J.* J. Biol. Chem., *164*, 321—328, 1946.
19. *Garilhe P., Laskowsky M. S.* Biophys. Biochim. Acta, *18*, 370–376, 1955
20. *Mesrob B. K., Stoeva S. P., Simeonova R. A.* Annal. Chem. Technol. Inst., *28*, 65—77, Sofia, 1981. (Engl.).
21. *Holmquist B., Vallee B.* Biochemistry, *15*, 101—107, 1976.
22. *Morihara K.* In: Adv. in Enzymology, *41*, 179, 1974.
23. *Fruton J.* In: Adv. in Enzymology, *33*, 401, 1970.
24. *Hill R. J.* Dairy Res., *36*, 409—415, 1969.
25. *Feder J.* Biochem. Biophys. Res. Comm., *32*, 326–332, 1968.
26. *Stoeva S. P., Dimitrova E. A., Atanasov B. P., Mesrob B. K.* FECS, 3—rd Conf. on Chem. and Biotech. of Biol. Active Nat. Prod., *4* 13–17, Sofia, 1985.
27. *Dietl T., Tschetsche H.* Z. Physiol. Chem., *357*, 121—125, 1976.
28. *Balls A., Jamsen E.* In: Adv. in Enzymology, *13*, 321–329, 1952.
29. *Riordan J., Sokolowsky M., Vallee B.* Biochemistry, 6, 258–261, 1967.
30. *Ovadi J., Libor S., Elődi P.* Acta. Biochem. Biophys. Acad. Sci. Hung., *2*, 445—459, 1967.

Received on the 5.1987 r.

Биолог. ж. Армении, т. 40, № 5, 366—373, 1987 УДК 517.16/17+612.43/45

СОДЕРЖАНИЕ ДОФА И ДОФАМИНА В НАДПОЧЕЧНИКАХ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ГИПОПАРАТИРЕОЗЕ

Д. Н. ХУДАВЕРДИН, Г. Г. БАКУНЦ

Ереванский государственный медицинский институт, кафедра физиологии, ЦНИЛ

Аннотация — Изучено содержание ДОФА и дофамина в надпочечниках крыс на 4-, 14- и 30-й дни экспериментального гипопаратиреоза. Показана динамика изменений этих показателей. Обобщены полученные данные и результаты биохимического изучения центральных и периферических моноаминергических систем, а также морфологического изучения надпочечников в динамике развития экспериментального гипопаратиреоза.

Ամփոփում — *Ուսումնասիրվել է ԴՈՖԱ-ի և դոֆամինի պարունակությունը առնետների մակերիկամներում փորձարարական ԲՀՀարվահանգեղձության 4-րդ, 14-րդ և 30-րդ օրերին.*

Ամփոփվել են կենտրոնական և պերիֆերիկ մոնոամիներգիկ համակարգերի ակտիվության կենսաքիմիական հետազոտության տվյալները և արդյունքները, ինչպես նաև կատարվել է մակերիկամների մորֆոլոգիական հետազոտություն փորձարարական ԲՀՀարվահանգեղձության զարգացման ամբողջ ընթացքում.

Abstract — The DOPA and dopamine content in the rat adrenal glands at the 4 th, 14 th, and 30 th days of the experimental hypoparathyreosis have been investigated. The data of the biochemical investigations of the central and periferic monoaminergic systems, and also with the morphological investigations of the adrenal glands under the experimental hypoparathyreosis conditions are summarized and discussed.

Ключевые слова: гипопаратиреоз, ДОФА, катехоламины, паратгормон, Ca^{2+}.

В настоящее время интенсивно изучаются нетрадиционные механизмы стресса, выдвинуто положение, согласно которому паратгормон, осуще-