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Hemoglobin as a Potential Source of Natural Regulatory Oligopeptides

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Abstract—Theoretical structure–function analysis of all possible hemoglobin molecule fragments was performed to determine sites that could be potential sources of regulatory oligopeptides. Known data on bovine hemoglobin primary structure and information of the EROP-Moscow database concerning structure and functions of natural oligopeptides were used along with a computer program complex. A total of 6750 natural non-hemoglobin oligopeptides with hemoglobin fragments of 2-14 amino acid residues were found. Structures of 20 of them were completely identical to hemoglobin fragments. Most of the revealed oligopeptides exhibit properties of neuropeptides, antimicrobial agents, and hormones. A number of them exhibit functions previously not known for hemoglobin fragments. The possibility of natural formation of regulatory oligopeptides from hemoglobin and other food protein molecules, generation of the exogenous oligopeptide pool, their participation in regulation processes as well as accordance of results obtained here with the oligopeptide continuum concepts are discussed.

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Key words: hemoglobin, fragment, neuropeptide, antimicrobial oligopeptide, EROP-Moscow database, continuum

It is known that natural regulatory oligopeptides are usually formed by splitting off from specialized precursors, and they contain from 2 to ~50 amino acid residues [1, 2]. The spectrum of their functional activities is diverse, but regulators of nervous and endocrine systems along with antimicrobial oligopeptides make up the bulk of known oligopeptides [3, 4].

At the same time, more and more facts appear showing that there are also oligopeptides in different organs and tissues of living organisms that are not formed from specialized precursors, but are rather natural fragments of well studied proteins. Functional role in an organism is not established for most. Studying functions of some of such fragments and of those obtained by experimental proteolysis has shown that they can serve as oligopeptide regulators. Thus, a number of fragments of milk proteins (casein [5-9], α-lactalbumin, β-lactoglobulin, and lactoferrin [10, 11]) as well of cytochrome *c* [12, 13] and hemoglobin [14-17] are able to exhibit opioid activity, i.e. they are neuropeptides. It is also known that some lactoferrin [18] and hemoglobin [19-21] fragments also exhibit antimicrobial activity.

Abbreviations: Hb, hemoglobin.

To date the largest number of fragments has been experimentally revealed for hemoglobin. In addition to already mentioned functions, these fragments can serve as hormones [22], enzyme inhibitors [23-25], and other regulators [21, 26, 27]. Multipotency was found for some of them. Thus, hemorphin-9 (site 31-39 of bovine hemoglobin β-chain) exhibits properties of neuropeptide and enzyme inhibitor [24].

However, up to the present time practically no systemic structural and functional investigations of protein fragments were have been carried out. Thus, we have carried out a theoretical structure–function analysis of all possible fragments of the hemoglobin molecule in order to identify its regions that could serve as potential sources of regulatory oligopeptides and to reveal their possible functions not previously known for hemoglobin oligopeptides.

MATERIALS AND METHODS

Primary structures of hemoglobin fragments were compared with amino acid sequences of presently known natural regulatory oligopeptides. The EROP-Moscow (**E**ndogenous **R**egulatory **O**ligo**P**eptides) database was

used as the source of such oligopeptides [4, 28]. By the time of investigation it contained information about structure and functions of 7145 natural oligopeptide regulators, most of which are formed from specialized precursors.

The EROP-Moscow database also contains data on 232 hemoglobin fragments identified in different organs and tissues of members of 13 mammalian species. The largest number of identified natural fragments belongs to bovine hemoglobin (111 structures). Its molecule consists of α- and β-chains (141 and 145 residues, respectively [29, 30]) whose homology is 38% (55 coinciding residues). Over 50 different natural fragments are known for each chain, and functional characteristics for some of them have been determined. That is why just this hemoglobin was chosen as the object of investigation.

Thus, the hemoglobin molecule, its natural fragments formed by proteolysis, and natural oligopeptides split off from specialized precursors are considered in this article.

Structure and function was analyzed using a computer program complex. Complete amino acid sequences of protein chains serving as a source of fragments of a certain length were inputted into the specially designed programs, step-by-step fragmentation was performed, and structures of the resulting fragments and all oligopeptides of the EROP-Moscow database were compared. Data on natural oligopeptides containing hemoglobin fragment(s) were automatically included into the table of results. Then these data were processed using standard programs for sorting and choosing groups of molecules according to certain structural and functional characteristics.

RESULTS

More than 132,807 cases of the hemoglobin dipeptide fragment incorporation into natural oligopeptide structures of the EROP-Moscow database are registered in the table. Evidently, all larger fragments contain overlapping dipeptide structures. Such a high value is explained by multiple repeats of the same natural oligopeptides containing different hemoglobin fragments. The majority of these oligopeptides are formed from specialized precursors and they are not protein fragments. However, during primary comparison of hemoglobin fragments with natural oligopeptide structures, these fragments were also noted in 232 natural hemoglobin fragments. After exclusion of these fragments and numerous non-hemoglobin oligopeptide repeats, there remained 6750 different structures containing one or more hemoglobin fragments (Fig. 1). It appears that they contain hemoglobin fragments of 2-14 amino acid residues. Practically all possible di- and tripeptides as well as larger hemoglobin fragments are registered in these oligopeptides obtained from members of all biological kingdoms.

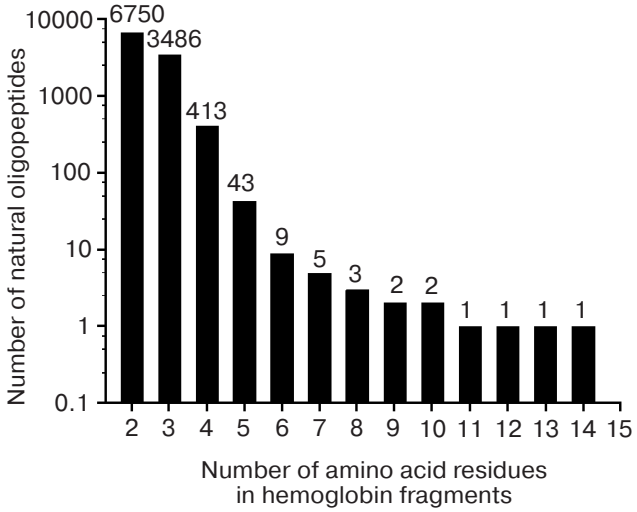


Fig. 1. Number of natural oligopeptides containing hemoglobin fragments.

The following specific peculiarities of natural oligopeptides containing hemoglobin fragments can be distinguished:

– the presence of single fragments of different length;

– the frequency of identical fragments in different hemoglobin chains (such as pig hemoglobin-like peptide S6 [31]);

– the presence of identical fragments in oligopeptides obtained from different biological species;

– the presence of two or more different fragments in one natural oligopeptide;

– almost complete overlapping of natural oligopeptide by hemoglobin fragment(s);

– complete structural coincidence of natural oligopeptide with hemoglobin fragment;

– functional diversity.

Because of the large number of natural oligopeptides containing hemoglobin fragments, it is impossible to show all of them. For this reason only structures containing sufficiently large structures, beginning from pentapeptides, are shown in Fig. 2 demonstrating most of the mentioned features.

Functional analysis of natural non-hemoglobin oligopeptides containing hemoglobin fragments has shown that they exhibit a broad spectrum of functional activity. Also, a single fragment can appear in oligopeptides belonging to several different functional classes. Functional diversity of some such oligopeptides is shown in Fig. 3.

Previous investigations of functional characteristics of natural hemoglobin oligopeptides mainly dealt with their neuropeptide, antimicrobial agent, hormone, enzyme inhibitor, and peptide potentiator properties. For this reason, we have distinguished data on the number of

Hb	*Fragment*	*EROP*	*F*	*Oligopeptide Name*	*Oligopeptide sequence*
α-Hb	LSAAD	E03590	UK	Venom peptide BmKn1 (scorpion)	FIGAVAGLLSKIFGKRSMRDMDTMKYLYDPS**LSAAD**LKTLQKLMENY
α-Hb	GKVGG	E03882	AM	Ponericin G6 (ant)	GLVDVL**GKVGG**LIKKLLP
α-Hb	GKVGG	E03883	AM	Ponericin G7 (ant)	GLVDVL**GKVGG**LIKKLLPG
α-Hb	EALER	E04696	NP	Peptide NLP-11-3 (nematode)	SPAISPAYQFENAFGLS**EALER**A
α-Hb	AKVAA	E02861	AM	Maculatin 1.1 (frog)	GLFGVL**AKVAA**HVVPAIAEHF
α-Hb	AKVAA	E02862	AM	Maculatin 1.1.1 (frog)	FGVL**AKVAA**HVVPAIAEHF
α-Hb	AAALT	E03167	AF	Antifreeze peptide (fish)	DTASDAAA**AAALT**AANAKAAAELTAANAAAAAAATAR
α-Hb	AAALT	E03166	AF	Antifreeze peptide 3 (fish)	DTASDAAA**AAALT**AANAAAAAKLTADNAAAAAAATAA
α-Hb	LSELS	E01419	HM	Cholecystokinin-like peptide (frog)	DLLASLTHEQKQLIMSQLLPEL**LSELS**NAEDHLHPMRDRDYAGWMDF
α-Hb	KLRVD	E06803	PP	Hemoglobin-like peptide S6 (pig)	**DLHA**Y**KLRVDPVNFKLLSH**
β-Hb	NFKLL	E06803	PP	Hemoglobin-like peptide S6 (pig)	DLHAYKLRVDPV**NFKLL**SH
α-Hb	LVTLA	E06782	PP	Hemoglobin-like peptide D8 (dog)	**LVTLA**CHHPTE**FTPAVHA**FAPKF
α-Hb	STVLT	E04377	AM	Entericidin B *(S. typhimurium)*	MVKKTIAAIFSVLVL**STVLT**ACNTTRGVGEDISDGGSAISGAATRAQQ
α-Hb	STVLT	E04373	AM	Entericidin B (*E. coli*)	MVKKTIAAIFSVLVL**STVLT**ACNTTRGVGEDISDGGNAISGAATKAQQ
β-Hb	EEKAA	E00739	HM	Glucagon like peptide 1 (frog)	HADGTFTSDMSSYL**EEKAA**KEFVDWLIKGRPK
β-Hb	EEKAA	E03850	HM	Glucagon-like peptide 1A (frog)	HAEGTYTNDVTQFL**EEKAA**KEFIDWLIKGKPK
β-Hb	EEKAA	E03849	HM	Glucagon-like peptide 1A (frog)	HAEGTYTNDVTQFL**EEKAA**KEFIDWLIKGKPKKLRLS
β-Hb	EEKAA	E02479	HM	Glucagon-like peptide 1 (frog)	HAEGTFTSDMTSYL**EEKAA**KEFVDWLIKGRPK
β-Hb	EEKAA	E02383	HM	Glucagon-like peptide 32 (toad)	HAEGTFTSDMTSFL**EEKAA**KEFVDWLIKGRPK
β-Hb	EEKAA	E02384	HM	Glucagon-like peptide 37 (toad)	HAEGTYTNDVTQFL**EEKAA**KEFIDWLLKGIPKKQRLS
β-Hb	EEKAA	E05350	HM	Glucagon-like peptide 1B 1 (frog)	HAEGTYTNDVTEYL**EEKAA**KEFIEWLIKGKPKKIRYS
β-Hb	EEKAA	E05351	HM	Glucagon-like peptide 1C 1 (frog)	HAEGTFTNDMTNYL**EEKAA**KEFVGWLIKGKPK
β-Hb	EEKAA	E05352	HM	Glucagon-like peptide 1C 2 (frog)	HAEGTFTNDMTNYL**EEKAA**KEFVGWLINGKPK
β-Hb	EEKAA	E02784	HM	Glucagon-like peptide 1 (frog)	HADGTYTNDVTQFL**EEKAA**KEFIDWILKGKPKKQRLS
β-Hb	EEKAA	E02220	HM	Glucagon-like peptide 1-37 (toad)	HADGSYTNDVTEYL**EEKAA**KEFINWLIKGKPTKMRYS
β-Hb	EEKAA	E02222	HM	Glucagon-like peptide 1B-32 (frog)	HAEGTYTNDVTEYL**EEKAA**KEFIEWLIKGKPK
β-Hb	GGEAL	E06792	PP	Hemoglobin-like peptide D19 (dog)	EED**GGEALGRLLV**
β-Hb	RLLVV	E01991	AS	Surfractant-associated peptide C (pig)	LRIPCCPVNLK**RLLVV**VVVV**VLVVV**VIVGALLMGL
β-Hb	LVVYP	E06799	PP	Hemoglobin-like peptide S2 (pig)	**LVVYP**ATQR
β-Hb	LVVYP	E06800	PP	Hemoglobin-like peptide S3 (pig)	**LVVYP**A**TQRFFE**
β-Hb	LVVYP	E06514	NP	Opioid peptide (tick)	**LVVYPWT**KM
β-Hb	GKKVL	E03841	AM	Nigrocin 2 (frog)	GLLSKVLGV**GKKVL**CGVSGLC
β-Hb	GKKVL	E06090	AM	Nigrocin-2GRb (frog)	GLFGKILGV**GKKVL**CGLSGMC
β-Hb	KVLDS	E02960	HM	Glucagon-like peptide 2 (fish)	HVDGSFTSDVN**KVLDS**LAAKEYLLWVMTSKTSG
β-Hb	LLGNV	E06804	PP	Hemoglobin-like peptide S7 (pig)	FR**LLGNVL**
β-Hb	FKLLG	E02189	AM	Clavanin D (tunicate)	A**FKLLG**RIIHHVGNFVHGFSHVF
β-Hb	GNVLV	E03034	HM	Cholecystokinin I-49 (frog)	SNI**GNVLV**KYLQQSRKAGPSGRYVVLPNRPIFDQPHRINDRDYMGWMDF
β-Hb	VLVVV	E02027	AS	Surfractant-associated peptide C (dog)	GIPCFPSSLKRLLIIVVVI**VLVVV**VIVGALLMGL
β-Hb	VVAGV	E02825	AM	Cecropin (mosquito)	GRLKKLGKKIEGAGKRVFKAAEKALP**VVAGV**KAL
β-Hb	VAGVA	E06005	AM	Lividin-1 (frog)	ILPF**VAGVA**AEMMQHVYCAASKKC
β-Hb	VAGVA	E02601	AM	Brevinin-1Sc (frog)	FFPI**VAGVA**GQVLKKIYCTISKKC
β-Hb	VVAGV	E01618	UK	Bioactive peptide (squirrel)	**VVAGVANA**
β-Hb	FQKVV	E06611	EI	Peptide 30-3 (pig)	**FQKVVA**K

Fig. 2. Pentapeptides and larger bovine hemoglobin fragments contained in natural oligopeptide structures. Names of α- and β-hemoglobin chains (α-Hb and β-Hb), fragment primary structure, accession number of natural oligopeptide in the EROP-Moscow database, its functional properties, name, source of isolation, and complete amino acid sequence in which fragment position is shown in bold are shown in succession. The standard one-letter code is used for designation of amino acid residues. The following abbreviations of functional classes are used: AF, antifreeze; AM, antimicrobial; EI, enzyme inhibitor; HM, hormone; NP, neuropeptide; PP, peptide potentiator; UK, unknown function.

natural non-hemoglobin oligopeptides having the same functions. These data shown in the table indicate that hemoglobin fragments are present in most such natural oligopeptides. Neuropeptides, antimicrobial agents, and hormones make up the bulk of them. The table also shows the number of known natural bovine hemoglobin fragments having these and some other functions.

Twenty primary structures, fully identical to possible hemoglobin fragments, were revealed among natural non-hemoglobin oligopeptides. Figure 4 shows all such oligopeptides among which there are 15 dipeptides, three tripeptides, one tetrapeptide, and one octapeptide (of hibernating ground squirrel [32]) with unknown function. In this case, some fragments in the hemoglobin molecule

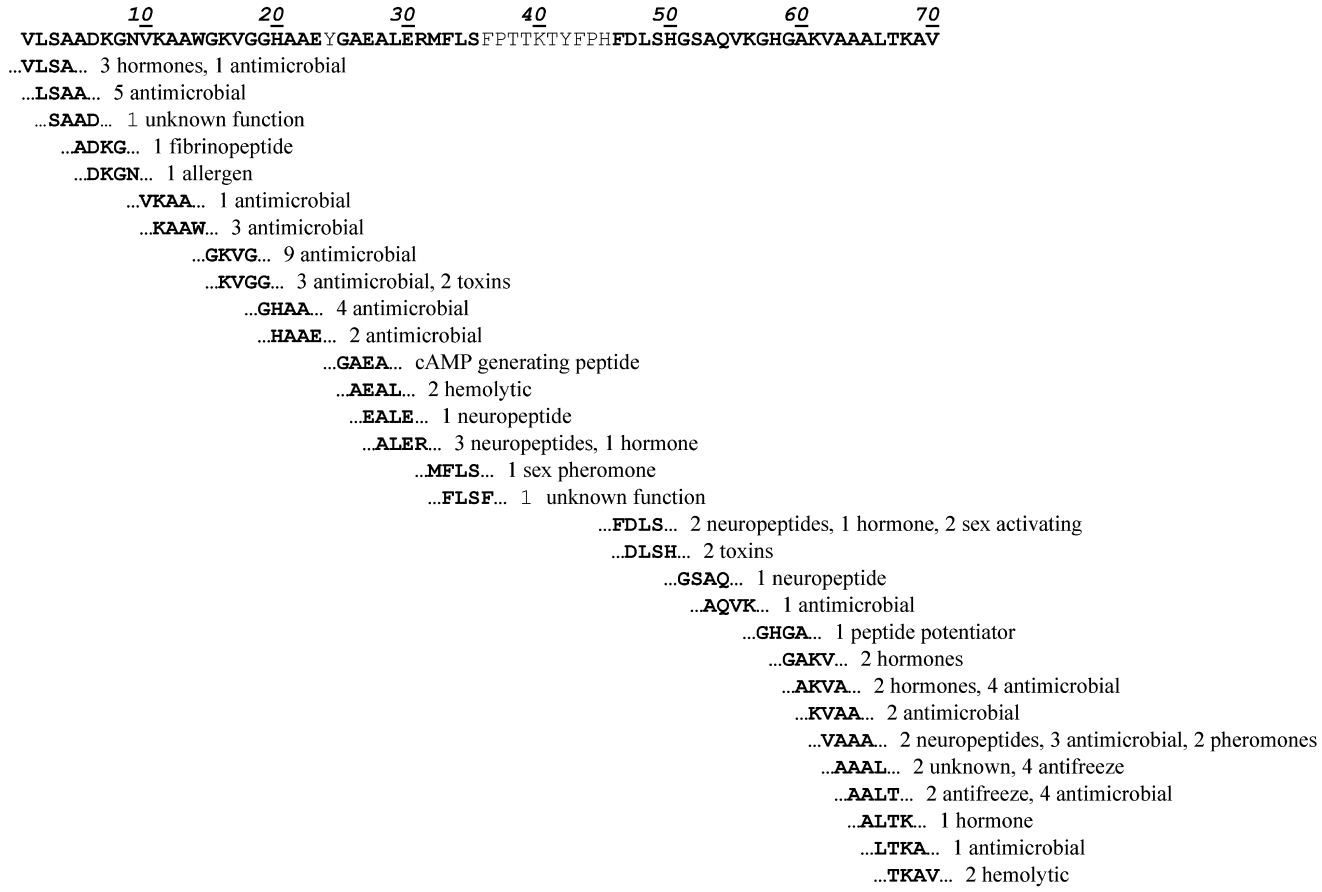
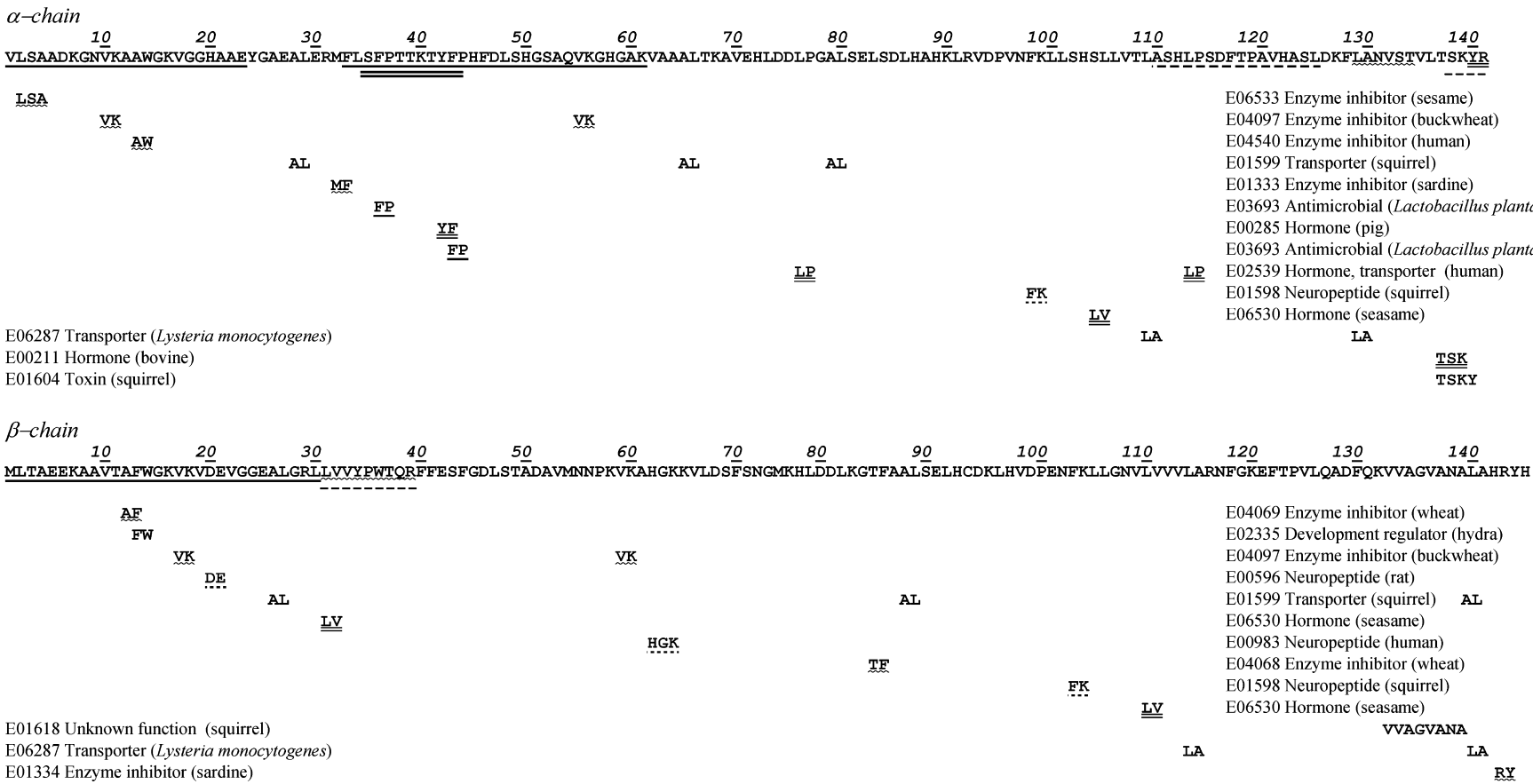


Fig. 3. Functional characteristics of natural oligopeptides containing tetrapeptide fragments of the N-terminal part of the hemoglobin α-chain. All tetrapeptide sites of natural oligopeptides and sites overlaying protein primary structure by them are shown in bold.

appear several times (for example, dipeptide AL exhibiting the transporter function is repeated six times). These natural non-hemoglobin oligopeptides are characterized by eight different type functions, five of which have been found experimentally in natural hemoglobin fragments. Figure 4 also shows several non-hemoglobin oligopeptides whose functions were not studied in natural hemoglobin oligopeptides (see also the table). Enzyme inhibitors were prevalent among them, and for one dipeptide LP (human serum amyloid A-derived peptide 6 [33])

Number of natural oligopeptides containing bovine hemoglobin fragments and exhibiting functions identical to those of natural hemoglobin fragments

No.	Functional class	Number of natural oligopeptides containing hemoglobin fragment(s), A	Number of oligopeptides contained in the EROP-Moscow database, B	A/B, %	Number of known natural bovine hemoglobin fragments
1	Neuropeptide	1619	1638	98.8	16
2	Antimicrobial	1459	1464	99.7	3
3	Hormone	1217	1227	99.2	2
4	Enzyme inhibitor	201	233	86.3	3
5	Peptide potentiator	54	58	93.1	1
6	Toxin	919	927	99.1	0
7	Development regulator	56	58	96.6	0
8	Transporter	3	4	75.0	0



Underlined: ANTIMICROBIAL, HORMONE, NEUROPEPTIDE, ENZYME INHIBITOR, PEPTIDE POTENTIATOR

Fig. 4. Complete coincidence of natural non-hemoglobin oligopeptide structures with possible hemoglobin fragments. Natural hemoglobin fragments with identified functional properties are distinguished by different underlining in primary structures of α- and β-chains of the hemoglobin molecule. Designations of belonging to a particular functional class are given in the figure. Among non-hemoglobin oligopeptides, only structures characterized by functional properties detected in natural hemoglobin fragments are underlined. The E00211 hormone was isolated from bovine pineal gland, and there are no data showing that it is a hemoglobin fragment.

NEUROPEPTIDES

TSKYR	**E00363 α-Hb 137-141 (bovine)**
YR	**E00240 α-Hb 140-141 (bovine) ***
JGMIGTL**TSK**RIKQ	E00781 (frog)
JAIV**SK**A**R**RPYIL	E02387 (toad)
SP**YR**AFAFA	E04625 (nematode)
LVVYP	**E01885 β-Hb 31-35 (bovine)**
LVVYPWT	**E01885 β-Hb 31-37 (bovine)**
LVVYPWTQ	**E01090 β-Hb 31-38 (bovine)**
LVVYPWTQR	**E01088 β-Hb 31-39 (bovine) ***
LVVYPWTQRF	**E00240 β-Hb 31-40 (bovine)**
VVYPW	**E01087 β-Hb 32-36 (bovine)**
VVYPWT	**E01086 β-Hb 32-37 (bovine) ***
VVYPWTQ	**E01091 β-Hb 32-38 (bovine)**
VVYPWTQRF	**E00289 β-Hb 32-40 (bovine)**
YPWTQR	**E06634 β-Hb 34-39 (bovine)**
YPWT	**E00612 β-Hb 34-37 (bovine)**
YPWTQ	**E00611 β-Hb 34-38 (bovine)**
YPWTQRF	**E06635 β-Hb 34-40 (bovine)**
YPWTQRFF	**E06636 β-Hb 34-41 (bovine)**
LVVYPWTKM	E06514 (tick)
YPWF	E02184 (human)

ANTIMICROBIAL

VLSAADKGNVKAAWGKVGGHAAE	**E06607 α-Hb 1-23 (bovine)**
AC**SA**G	E05756 (worm)
GFRDVL**KG**AA**KA**FVKT**V**A**GH**I**A**N	E05521 (frog)
GIGASI**LSAA**KV**G**LKGL**A**K**G**LAEHF**A**Nz	E01308 (toad)
FLSFPTTKTYFPHFDLSHGSAQVKGHGAK	**E06681 α-Hb 33-61 (bovine)**
FP	E03693 (*Lactobacillus plantarum*)
KRH**HG**Y**K**	E04147 (human)
MLTAEEKAAVTAFWGKVKVDEVGGEALGRL	**E06607 β-Hb 1-30 (bovine)**
KGL**AE**HF**A**D	E01400 (toad)

HORMONES

SFPTTKTYFP	**E00240 α-Hb 35-44 (bovine)**
YF	E03693 (pig)
YR	**E00240 α-Hb 140-141 (bovine) ***
G**YR**FS	E04026 (cow cockle)

ENZYME INHIBITORS

LANVST	**E00755 α-Hb 129-134 (bovine)**
AVTDNEIVPQC**LAN**G**SK**CYSHDVCCTKRCHNYAKKCVT	E01317 (house fly)
LVVYPWTQR	**E01088 β-Hb 31-39 (bovine) ***
VVYPWT	**E01086 β-Hb 32-37 (bovine) ***
R**VY**	E01341 (sardine)
I**VY**	E04070 (wheat)
L**VY**	E04070 (sesame)
L**YP**	E01441 (bonito)

PEPTIDE POTENTIATORS

ASHLPSDFTPAVHASL	**E06606 α-Hb 110-125 (bovine)**
LVTL**AC**H**H**P**T**E**FTPAVHA**FAPKF	E06782 (dog)

Fig. 5. Partial structural coincidence of natural non-hemoglobin oligopeptides and possible hemoglobin fragments. All natural hemoglobin fragments are marked in bold. The asterisk points to natural hemoglobin fragments for which it is known that they belong to two functional classes. Pyroglutaminyl at N-terminus of amino acid sequences is designated by J.

two types of functional activity (hormone and transporter) are known. However, functional similarity of such non-hemoglobin oligopeptides and natural hemoglobin fragments containing these oligopeptides was registered only in two dipeptides, antimicrobial FP and hormone YF. It was also shown that some of these natural oligopeptides exhibit functions that were not studied in natural hemoglobin fragments.

Natural oligopeptides were also separately isolated from the EROP-Moscow database that were structurally maximally similar to natural hemoglobin fragments and had identical functions. For some of them structural similarity was more than 50% (Fig. 5).

DISCUSSION

Evidently, after entering an organism with food, proteins are cleaved in a natural way by proteolytic enzymes, and protein fragments are formed. Hemoglobin is an example, and its fragments become exogenous oligopeptides. Owing to homology of its α- and β-chains and due to repetition of the same parts of the amino acid sequence within one chain, small fragments (di- and tripeptides) can be formed in significant amounts and influence different regulatory processes. In particular, detection of enzyme inhibitors among them shows that cleavage of food proteins can be inhibited by proteolysis products.

No functionally characterized hemoglobin fragments which were longer than tetrapeptides were found among natural non-hemoglobin oligopeptides. However, it is known that rather small natural oligopeptide fragments exhibit functional properties of the whole molecule. Thus, mammalian β-endorphin containing 31 amino acid residues [34] shares the opioid function with its N-terminal natural pentapeptide fragment known as met-enkephalin [35]. The undecapeptide C-terminal fragment of pardaxin [36], whose complete structure consists of 33 amino acid residues [37], also retains its antimicrobial activity. We obtained a similar result for antimicrobial structures α-Hb 33-61 and 36-37 as well as for hormones α-Hb 35-44 and 42-43 (Figs. 4 and 5). Therefore, the hemoglobin fragment frequency in non-hemoglobin oligopeptides, exhibiting a certain function, can be indicative of the same type activity in this fragment. The detection of a minimal active site in regulatory molecules using the described data would make it possible to decrease the labor-consuming work on synthesis and testing of many natural oligopeptide fragments.

However, there are data showing that natural fragments of well-known proteins and oligopeptides can have not only functions of the mother molecule, but different functional properties as well. Thus, the N-terminal fragment (13 amino acid residues) of adrenocorticotropic hormone (ACTH) consisting in mammals of 39 residues [38] does not possess ACTH function, but exhibits function of melanocyte-stimulating hormone [39, 40]. Examples of changes in functional properties of hemoglobin fragments upon change in their size are also noted in this work in Fig. 4. In particular, it is known that a noticeable functional peculiarity of oligopeptides TSK and TSKY is that they, being fragments of neuropeptide TSKYR (neokyotorphin, α-Hb 137-141 [41]), can exhibit hormone [42] and toxin [32] activity, respectively. At the same time, the initial part of its structure (TSK) was found in many natural functionally different oligopeptides, including neuropeptides, while the second part (YR), the α-Hb fragment 140-141, is known as the neuropeptide kyotorphin [43].

The data obtained show that hemoglobin fragments can have one or more functions not specific to the original molecule and exhibit functional diversity. Natural fragmentation of hemoglobin and other proteins can result in formation in the organism of a dynamically developing pool of exogenous regulatory oligopeptides whose functions may change during formation of smaller peptide structures. This results in more or less gradual transitions of biological activity spectra providing for any admissible combinations of effects on the organism's functions. The existence of the endogenous/exogenous pool of regulatory molecules makes it possible to expand the sense and content of a hypothesis concerning the functionally continuous population (continuum) of natural oligopeptides [44].

So far, little is known about the targets available in the gastrointestinal tract for particular neuropeptides and hormones and what the ability of these structures to penetrate into other organs and tissues is. However, it is evident that the access to targets is possible for antimicrobial protein fragments that contact microflora of the tract and might inhibit their activity. Experimental data show that natural concentrations of hemoglobin fragments may reach several micromolar [21]. The inhibitory activity of some hemoglobin fragments towards bacteria is characterized by the same concentrations [19]. Therefore, the participation in this process (which is the component of immune regulation [45]) of food protein fragments, in particular, those of hemoglobin, as well of enzymes entering the organism with food is possible [46].

It should be noted in conclusion once more that by the present only a small number of the possible natural protein fragments have been identified in living organisms, and functional properties of only a few of them have been determined. The revealing of natural oligopeptides formed from specialized precursors is also far from complete. Also, only a single function was studied in most of them, whereas they may be multipotent. Every year our knowledge is supplemented with several hundreds of new natural oligopeptide structures [4]. Therefore, further accumulation of data on their structure and functions will make possible more complete characterization of func-

tional abilities of numerous, yet not studied, protein fragments and the use of these data in practice, e.g. in dietetics.

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