

CYCLIC PEPTIDE COMPOUND AND USE THEREOF

REFERENCE TO RELATED APPLICATION

5 The present application claims priority to Chinese Patent Application CN 202311247312.8 filed on September 25, 2023 and Chinese Patent Application CN 202411310856.9 filed on September 19, 2024, the contents of which are incorporated herein by reference in their entirety and for all purposes.

TECHNICAL FIELD

10 The present invention relates to the field of biomedicine or the field of cosmetic products, specifically to cyclic peptide compounds and uses thereof.

BACKGROUND ART

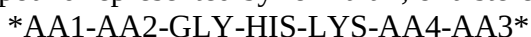
15 GHK is a tripeptide molecule, also known as tripeptide or tripeptide-1, with a sequence of glycyl-histidyl-lysine, which is a hydrolysate of collagen. It is naturally found in the blood, saliva and urine of a person. GHK is known for its ability to promote production of type I collagen fragments. Its mechanism of action can be simply understood as when a collagen protein is naturally decomposed in skin, the resulting peptide fragments signal to the skin that it should start working and produce
20 some pretty new collagen proteins.

GHK has a high affinity for a divalent copper ion, and can spontaneously bind to the divalent copper ion to form a complex GHK-Cu, the latter is also known as the blue-copper peptide because of the blue colour of the aqueous solution and is the main form of GHK that exerts efficacy in vivo. Its functions mainly include: (1) the
25 chemotaxis of repairing cells, such as macrophages, mast cells, capillary cells; (2) anti-inflammatory effects (inhibiting free radicals, thromboxane formation, transforming growth factor beta-1, tumor necrosis factor alpha, and protein glycation, simultaneously increasing superoxide dismutase, dilating blood vessels, blocking UV damage to cutaneous keratinocytes, and improving fibroblast recovery after X-ray therapy, etc.); (3) increasing the synthesis of collagen proteins, elastin,
30 hyaluronic acid, metalloprotease, anti-protease, vascular endothelial growth factor, fibroblast growth factor 2, nerve growth factor, neutrophil 3 and neutrophil 4, and erythropoietin; (4) increasing the proliferation of fibroblasts and keratinocytes; nerve growth, angiogenesis, and hair follicle size. Control studies of aged skin
35 showed that GHK-Cu can tighten the skin, improve elasticity and compactness, and reduce fine lines, wrinkles, photo-damages and hyperpigmentation, and can also promote hair growth and improve the success rate of hair transplantation.

SUMMARY OF THE INVENTION

40 The present invention provides a cyclic peptide compound having a novel structure and an efficacy comparable to or even better than that of GHK tripeptide, and use of said cyclic peptide compound in a dermatological or cosmetic composition for stimulating hair growth or anti-aging of the skin.

45 For this reason, in a first aspect of the invention, the present invention provides a cyclic peptide compound represented by formula I, or a stereoisomer thereof,



Formula I

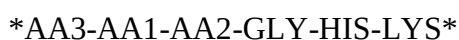
wherein:

AA1 is an amino acid residue;

50 AA2 is absent or is an amino acid residue;

- AA3 is an amino acid residue;
 AA4 is absent or is an amino acid residue;
 * indicates that the N-terminus and the C-terminus of formula I are linked to form a cyclic peptide;
- 5 the amino acid is a natural amino acid or a non-natural amino acid;
 the amino acid is of D-configuration or L-configuration.
 It should be noted that the formula I has the N-terminus on the left side and the C-terminus on the right side.
- In some embodiments, the amino acid is of L-configuration.
- 10 In some embodiments, the amino acid is a natural amino acid.
 In some embodiments, the amino acid is a hydrophobic natural amino acid.
 In some embodiments, the amino acid is selected from the group consisting of alanine (ALA; A), glycine (GLY; G), isoleucine (ILE; I), leucine (LEU; L), methionine (MET; M), phenylalanine (PHE; F), proline (PRO; P), tryptophan (TRP; W), and valine (VAL; V).
- 15 In some embodiments, AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue.
- 20 In some embodiments, AA1 is selected from the group consisting of an alanine residue, a methionine residue, a phenylalanine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a glycine residue.
 In some embodiments, AA1 is selected from the group consisting of a methionine residue, an alanine residue, a phenylalanine residue, a glycine residue, and a proline residue.
- 25 In some embodiments, AA2 is an amino acid residue.
 In some embodiments, AA2 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue.
- 30 In some embodiments, AA2 is selected from the group consisting of a valine residue, a proline residue, a leucine residue, an alanine residue, an isoleucine residue, a methionine residue, and a tryptophan residue.
 In some embodiments, AA2 is selected from the group consisting of a proline residue, a leucine residue, a valine residue, an isoleucine residue, and a tryptophan residue.
- 35 In some embodiments, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue.
- 40 In some embodiments, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a glycine residue, and a valine residue.
 In some embodiments, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, an isoleucine residue, and a valine residue.
- 45 In some embodiments, AA3 is selected from the group consisting of an isoleucine residue, a leucine residue, a phenylalanine residue, a methionine residue, and a valine residue.
- 50 In some embodiments, AA4 is absent.

In some embodiments, the cyclic peptide compound has a structure represented by formula I-1,



Formula I-1

5 wherein:

AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;
and/or

10 AA2 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;
and/or

15 AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

* indicates that the N-terminus and the C-terminus of the formula I-1 are linked to form a cyclic peptide;

the amino acid is of D-configuration or L-configuration.

20 It should be noted that the formula I-1 has the N-terminus on the left side and the C-terminus on the right side.

In some embodiments, the amino acid is of L-configuration.

25 In some embodiments, AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a glycine residue.

In some embodiments, AA1 is selected from the group consisting of a methionine residue, an alanine residue, a phenylalanine residue, a glycine residue, and a proline residue.

30 In some embodiments, AA2 is selected from the group consisting of an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a valine residue.

In some embodiments, AA2 is selected from the group consisting of a proline residue, a leucine residue, a valine residue, an isoleucine residue, and a tryptophan residue.

35 In some embodiments, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a glycine residue, and a valine residue.

40 In some embodiments, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, an isoleucine residue, and a valine residue.

In some embodiments, AA3 is selected from the group consisting of an isoleucine residue, a leucine residue, a phenylalanine residue, a methionine residue, and a valine residue.

45 In some embodiments, the structural formula of the cyclic peptide compound is as shown in Table A.

Table A: The structural formula of the cyclic peptide compound (all amino acids are of L-configuration)

SEQ ID NO:	The structural formula of the cyclic peptide compound
1	ALA ALA ALA GLY HIS LYS

2	ALA ALA GLY GLY HIS LYS
3	ALA ALA ILE GLY HIS LYS
4	ALA ALA LEU GLY HIS LYS
5	ALA ALA MET GLY HIS LYS
6	ALA ALA PHE GLY HIS LYS
7	ALA ALA PRO GLY HIS LYS
8	ALA ALA TRP GLY HIS LYS
9	ALA ALA VAL GLY HIS LYS
10	ALA GLY ALA GLY HIS LYS
11	ALA GLY GLY GLY HIS LYS
12	ALA GLY ILE GLY HIS LYS
13	ALA GLY LEU GLY HIS LYS
14	ALA GLY MET GLY HIS LYS
15	ALA GLY PHE GLY HIS LYS
16	ALA GLY PRO GLY HIS LYS
17	ALA GLY TRP GLY HIS LYS
18	ALA GLY VAL GLY HIS LYS
19	ALA ILE ALA GLY HIS LYS
20	ALA ILE GLY GLY HIS LYS
21	ALA ILE ILE GLY HIS LYS
22	ALA ILE LEU GLY HIS LYS
23	ALA ILE MET GLY HIS LYS
24	ALA ILE PHE GLY HIS LYS
25	ALA ILE PRO GLY HIS LYS
26	ALA ILE TRP GLY HIS LYS
27	ALA ILE VAL GLY HIS LYS
28	ALA LEU ALA GLY HIS LYS
29	ALA LEU GLY GLY HIS LYS
30	ALA LEU ILE GLY HIS LYS
31	ALA LEU LEU GLY HIS LYS
32	ALA LEU MET GLY HIS LYS
33	ALA LEU PHE GLY HIS LYS
34	ALA LEU PRO GLY HIS LYS
35	ALA LEU TRP GLY HIS LYS
36	ALA LEU VAL GLY HIS LYS
37	ALA MET ALA GLY HIS LYS
38	ALA MET GLY GLY HIS LYS
39	ALA MET ILE GLY HIS LYS
40	ALA MET LEU GLY HIS LYS
41	ALA MET MET GLY HIS LYS
42	ALA MET PHE GLY HIS LYS
43	ALA MET PRO GLY HIS LYS
44	ALA MET TRP GLY HIS LYS
45	ALA MET VAL GLY HIS LYS
46	ALA PHE ALA GLY HIS LYS
47	ALA PHE GLY GLY HIS LYS
48	ALA PHE ILE GLY HIS LYS
49	ALA PHE LEU GLY HIS LYS

50	ALA PHE MET GLY HIS LYS
51	ALA PHE PHE GLY HIS LYS
52	ALA PHE PRO GLY HIS LYS
53	ALA PHE TRP GLY HIS LYS
54	ALA PHE VAL GLY HIS LYS
55	ALA PRO ALA GLY HIS LYS
56	ALA PRO GLY GLY HIS LYS
57	ALA PRO ILE GLY HIS LYS
58	ALA PRO LEU GLY HIS LYS
59	ALA PRO MET GLY HIS LYS
60	ALA PRO PHE GLY HIS LYS
61	ALA PRO PRO GLY HIS LYS
62	ALA PRO TRP GLY HIS LYS
63	ALA PRO VAL GLY HIS LYS
64	ALA TRP ALA GLY HIS LYS
65	ALA TRP GLY GLY HIS LYS
66	ALA TRP ILE GLY HIS LYS
67	ALA TRP LEU GLY HIS LYS
68	ALA TRP MET GLY HIS LYS
69	ALA TRP PHE GLY HIS LYS
70	ALA TRP PRO GLY HIS LYS
71	ALA TRP TRP GLY HIS LYS
72	ALA TRP VAL GLY HIS LYS
73	ALA VAL ALA GLY HIS LYS
74	ALA VAL GLY GLY HIS LYS
75	ALA VAL ILE GLY HIS LYS
76	ALA VAL LEU GLY HIS LYS
77	ALA VAL MET GLY HIS LYS
78	ALA VAL PHE GLY HIS LYS
79	ALA VAL PRO GLY HIS LYS
80	ALA VAL TRP GLY HIS LYS
81	ALA VAL VAL GLY HIS LYS
82	GLY ALA ALA GLY HIS LYS
83	GLY ALA GLY GLY HIS LYS
84	GLY ALA ILE GLY HIS LYS
85	GLY ALA LEU GLY HIS LYS
86	GLY ALA MET GLY HIS LYS
87	GLY ALA PHE GLY HIS LYS
88	GLY ALA PRO GLY HIS LYS
89	GLY ALA TRP GLY HIS LYS
90	GLY ALA VAL GLY HIS LYS
91	GLY GLY ALA GLY HIS LYS
92	GLY GLY GLY GLY HIS LYS
93	GLY GLY ILE GLY HIS LYS
94	GLY GLY LEU GLY HIS LYS
95	GLY GLY MET GLY HIS LYS
96	GLY GLY PHE GLY HIS LYS
97	GLY GLY PRO GLY HIS LYS

98	GLY GLY TRP GLY HIS LYS
99	GLY GLY VAL GLY HIS LYS
100	GLY ILE ALA GLY HIS LYS
101	GLY ILE GLY GLY HIS LYS
102	GLY ILE ILE GLY HIS LYS
103	GLY ILE LEU GLY HIS LYS
104	GLY ILE MET GLY HIS LYS
105	GLY ILE PHE GLY HIS LYS
106	GLY ILE PRO GLY HIS LYS
107	GLY ILE TRP GLY HIS LYS
108	GLY ILE VAL GLY HIS LYS
109	GLY LEU ALA GLY HIS LYS
110	GLY LEU GLY GLY HIS LYS
111	GLY LEU ILE GLY HIS LYS
112	GLY LEU LEU GLY HIS LYS
113	GLY LEU MET GLY HIS LYS
114	GLY LEU PHE GLY HIS LYS
115	GLY LEU PRO GLY HIS LYS
116	GLY LEU TRP GLY HIS LYS
117	GLY LEU VAL GLY HIS LYS
118	GLY MET ALA GLY HIS LYS
119	GLY MET GLY GLY HIS LYS
120	GLY MET ILE GLY HIS LYS
121	GLY MET LEU GLY HIS LYS
122	GLY MET MET GLY HIS LYS
123	GLY MET PHE GLY HIS LYS
124	GLY MET PRO GLY HIS LYS
125	GLY MET TRP GLY HIS LYS
126	GLY MET VAL GLY HIS LYS
127	GLY PHE ALA GLY HIS LYS
128	GLY PHE GLY GLY HIS LYS
129	GLY PHE ILE GLY HIS LYS
130	GLY PHE LEU GLY HIS LYS
131	GLY PHE MET GLY HIS LYS
132	GLY PHE PHE GLY HIS LYS
133	GLY PHE PRO GLY HIS LYS
134	GLY PHE TRP GLY HIS LYS
135	GLY PHE VAL GLY HIS LYS
136	GLY PRO ALA GLY HIS LYS
137	GLY PRO GLY GLY HIS LYS
138	GLY PRO ILE GLY HIS LYS
139	GLY PRO LEU GLY HIS LYS
140	GLY PRO MET GLY HIS LYS
141	GLY PRO PHE GLY HIS LYS
142	GLY PRO PRO GLY HIS LYS
143	GLY PRO TRP GLY HIS LYS
144	GLY PRO VAL GLY HIS LYS
145	GLY TRP ALA GLY HIS LYS

146	GLY TRP GLY GLY HIS LYS
147	GLY TRP ILE GLY HIS LYS
148	GLY TRP LEU GLY HIS LYS
149	GLY TRP MET GLY HIS LYS
150	GLY TRP PHE GLY HIS LYS
151	GLY TRP PRO GLY HIS LYS
152	GLY TRP TRP GLY HIS LYS
153	GLY TRP VAL GLY HIS LYS
154	GLY VAL ALA GLY HIS LYS
155	GLY VAL GLY GLY HIS LYS
156	GLY VAL ILE GLY HIS LYS
157	GLY VAL LEU GLY HIS LYS
158	GLY VAL MET GLY HIS LYS
159	GLY VAL PHE GLY HIS LYS
160	GLY VAL PRO GLY HIS LYS
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183	ILE ILE ILE GLY HIS LYS
184	ILE ILE LEU GLY HIS LYS
185	ILE ILE MET GLY HIS LYS
186	ILE ILE PHE GLY HIS LYS
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188	ILE ILE TRP GLY HIS LYS
189	ILE ILE VAL GLY HIS LYS
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196	ILE LEU PRO GLY HIS LYS
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198	ILE LEU VAL GLY HIS LYS
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202	ILE MET LEU GLY HIS LYS
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232	ILE TRP PRO GLY HIS LYS
233	ILE TRP TRP GLY HIS LYS
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238	ILE VAL LEU GLY HIS LYS
239	ILE VAL MET GLY HIS LYS
240	ILE VAL PHE GLY HIS LYS
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242	ILE VAL TRP GLY HIS LYS
243	ILE VAL VAL GLY HIS LYS
244	LEU ALA ALA GLY HIS LYS
245	LEU ALA GLY GLY HIS LYS
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247	LEU ALA LEU GLY HIS LYS
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268	LEU ILE PRO GLY HIS LYS
269	LEU ILE TRP GLY HIS LYS
270	LEU ILE VAL GLY HIS LYS
271	LEU LEU ALA GLY HIS LYS
272	LEU LEU GLY GLY HIS LYS
273	LEU LEU ILE GLY HIS LYS
274	LEU LEU LEU GLY HIS LYS
275	LEU LEU MET GLY HIS LYS
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278	LEU LEU TRP GLY HIS LYS
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282	LEU MET ILE GLY HIS LYS
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284	LEU MET MET GLY HIS LYS
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290	LEU PHE GLY GLY HIS LYS
291	LEU PHE ILE GLY HIS LYS
292	LEU PHE LEU GLY HIS LYS
293	LEU PHE MET GLY HIS LYS
294	LEU PHE PHE GLY HIS LYS
295	LEU PHE PRO GLY HIS LYS
296	LEU PHE TRP GLY HIS LYS
297	LEU PHE VAL GLY HIS LYS
298	LEU PRO ALA GLY HIS LYS
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305	LEU PRO TRP GLY HIS LYS
306	LEU PRO VAL GLY HIS LYS
307	LEU TRP ALA GLY HIS LYS
308	LEU TRP GLY GLY HIS LYS
309	LEU TRP ILE GLY HIS LYS
310	LEU TRP LEU GLY HIS LYS
311	LEU TRP MET GLY HIS LYS
312	LEU TRP PHE GLY HIS LYS
313	LEU TRP PRO GLY HIS LYS
314	LEU TRP TRP GLY HIS LYS
315	LEU TRP VAL GLY HIS LYS
316	LEU VAL ALA GLY HIS LYS
317	LEU VAL GLY GLY HIS LYS
318	LEU VAL ILE GLY HIS LYS
319	LEU VAL LEU GLY HIS LYS
320	LEU VAL MET GLY HIS LYS
321	LEU VAL PHE GLY HIS LYS
322	LEU VAL PRO GLY HIS LYS
323	LEU VAL TRP GLY HIS LYS
324	LEU VAL VAL GLY HIS LYS
325	MET ALA ALA GLY HIS LYS
326	MET ALA GLY GLY HIS LYS
327	MET ALA ILE GLY HIS LYS
328	MET ALA LEU GLY HIS LYS
329	MET ALA MET GLY HIS LYS
330	MET ALA PHE GLY HIS LYS
331	MET ALA PRO GLY HIS LYS
332	MET ALA TRP GLY HIS LYS
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334	MET GLY ALA GLY HIS LYS
335	MET GLY GLY GLY HIS LYS
336	MET GLY ILE GLY HIS LYS
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338	MET GLY MET GLY HIS LYS
339	MET GLY PHE GLY HIS LYS
340	MET GLY PRO GLY HIS LYS
341	MET GLY TRP GLY HIS LYS
342	MET GLY VAL GLY HIS LYS
343	MET ILE ALA GLY HIS LYS
344	MET ILE GLY GLY HIS LYS
345	MET ILE ILE GLY HIS LYS
346	MET ILE LEU GLY HIS LYS
347	MET ILE MET GLY HIS LYS
348	MET ILE PHE GLY HIS LYS
349	MET ILE PRO GLY HIS LYS
350	MET ILE TRP GLY HIS LYS
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352	MET LEU ALA GLY HIS LYS
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354	MET LEU ILE GLY HIS LYS
355	MET LEU LEU GLY HIS LYS
356	MET LEU MET GLY HIS LYS
357	MET LEU PHE GLY HIS LYS
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360	MET LEU VAL GLY HIS LYS
361	MET MET ALA GLY HIS LYS
362	MET MET GLY GLY HIS LYS
363	MET MET ILE GLY HIS LYS
364	MET MET LEU GLY HIS LYS
365	MET MET MET GLY HIS LYS
366	MET MET PHE GLY HIS LYS
367	MET MET PRO GLY HIS LYS
368	MET MET TRP GLY HIS LYS
369	MET MET VAL GLY HIS LYS
370	MET PHE ALA GLY HIS LYS
371	MET PHE GLY GLY HIS LYS
372	MET PHE ILE GLY HIS LYS
373	MET PHE LEU GLY HIS LYS
374	MET PHE MET GLY HIS LYS
375	MET PHE PHE GLY HIS LYS
376	MET PHE PRO GLY HIS LYS
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378	MET PHE VAL GLY HIS LYS
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380	MET PRO GLY GLY HIS LYS
381	MET PRO ILE GLY HIS LYS
382	MET PRO LEU GLY HIS LYS
383	MET PRO MET GLY HIS LYS
384	MET PRO PHE GLY HIS LYS
385	MET PRO PRO GLY HIS LYS

386	MET PRO TRP GLY HIS LYS
387	MET PRO VAL GLY HIS LYS
388	MET TRP ALA GLY HIS LYS
389	MET TRP GLY GLY HIS LYS
390	MET TRP ILE GLY HIS LYS
391	MET TRP LEU GLY HIS LYS
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399	MET VAL ILE GLY HIS LYS
400	MET VAL LEU GLY HIS LYS
401	MET VAL MET GLY HIS LYS
402	MET VAL PHE GLY HIS LYS
403	MET VAL PRO GLY HIS LYS
404	MET VAL TRP GLY HIS LYS
405	MET VAL VAL GLY HIS LYS
406	PHE ALA ALA GLY HIS LYS
407	PHE ALA GLY GLY HIS LYS
408	PHE ALA ILE GLY HIS LYS
409	PHE ALA LEU GLY HIS LYS
410	PHE ALA MET GLY HIS LYS
411	PHE ALA PHE GLY HIS LYS
412	PHE ALA PRO GLY HIS LYS
413	PHE ALA TRP GLY HIS LYS
414	PHE ALA VAL GLY HIS LYS
415	PHE GLY ALA GLY HIS LYS
416	PHE GLY GLY GLY HIS LYS
417	PHE GLY ILE GLY HIS LYS
418	PHE GLY LEU GLY HIS LYS
419	PHE GLY MET GLY HIS LYS
420	PHE GLY PHE GLY HIS LYS
421	PHE GLY PRO GLY HIS LYS
422	PHE GLY TRP GLY HIS LYS
423	PHE GLY VAL GLY HIS LYS
424	PHE ILE ALA GLY HIS LYS
425	PHE ILE GLY GLY HIS LYS
426	PHE ILE ILE GLY HIS LYS
427	PHE ILE LEU GLY HIS LYS
428	PHE ILE MET GLY HIS LYS
429	PHE ILE PHE GLY HIS LYS
430	PHE ILE PRO GLY HIS LYS
431	PHE ILE TRP GLY HIS LYS
432	PHE ILE VAL GLY HIS LYS
433	PHE LEU ALA GLY HIS LYS

434	PHE LEU GLY GLY HIS LYS
435	PHE LEU ILE GLY HIS LYS
436	PHE LEU LEU GLY HIS LYS
437	PHE LEU MET GLY HIS LYS
438	PHE LEU PHE GLY HIS LYS
439	PHE LEU PRO GLY HIS LYS
440	PHE LEU TRP GLY HIS LYS
441	PHE LEU VAL GLY HIS LYS
442	PHE MET ALA GLY HIS LYS
443	PHE MET GLY GLY HIS LYS
444	PHE MET ILE GLY HIS LYS
445	PHE MET LEU GLY HIS LYS
446	PHE MET MET GLY HIS LYS
447	PHE MET PHE GLY HIS LYS
448	PHE MET PRO GLY HIS LYS
449	PHE MET TRP GLY HIS LYS
450	PHE MET VAL GLY HIS LYS
451	PHE PHE ALA GLY HIS LYS
452	PHE PHE GLY GLY HIS LYS
453	PHE PHE ILE GLY HIS LYS
454	PHE PHE LEU GLY HIS LYS
455	PHE PHE MET GLY HIS LYS
456	PHE PHE PHE GLY HIS LYS
457	PHE PHE PRO GLY HIS LYS
458	PHE PHE TRP GLY HIS LYS
459	PHE PHE VAL GLY HIS LYS
460	PHE PRO ALA GLY HIS LYS
461	PHE PRO GLY GLY HIS LYS
462	PHE PRO ILE GLY HIS LYS
463	PHE PRO LEU GLY HIS LYS
464	PHE PRO MET GLY HIS LYS
465	PHE PRO PHE GLY HIS LYS
466	PHE PRO PRO GLY HIS LYS
467	PHE PRO TRP GLY HIS LYS
468	PHE PRO VAL GLY HIS LYS
469	PHE TRP ALA GLY HIS LYS
470	PHE TRP GLY GLY HIS LYS
471	PHE TRP ILE GLY HIS LYS
472	PHE TRP LEU GLY HIS LYS
473	PHE TRP MET GLY HIS LYS
474	PHE TRP PHE GLY HIS LYS
475	PHE TRP PRO GLY HIS LYS
476	PHE TRP TRP GLY HIS LYS
477	PHE TRP VAL GLY HIS LYS
478	PHE VAL ALA GLY HIS LYS
479	PHE VAL GLY GLY HIS LYS
480	PHE VAL ILE GLY HIS LYS
481	PHE VAL LEU GLY HIS LYS

482	PHE VAL MET GLY HIS LYS
483	PHE VAL PHE GLY HIS LYS
484	PHE VAL PRO GLY HIS LYS
485	PHE VAL TRP GLY HIS LYS
486	PHE VAL VAL GLY HIS LYS
487	PRO ALA ALA GLY HIS LYS
488	PRO ALA GLY GLY HIS LYS
489	PRO ALA ILE GLY HIS LYS
490	PRO ALA LEU GLY HIS LYS
491	PRO ALA MET GLY HIS LYS
492	PRO ALA PHE GLY HIS LYS
493	PRO ALA PRO GLY HIS LYS
494	PRO ALA TRP GLY HIS LYS
495	PRO ALA VAL GLY HIS LYS
496	PRO GLY ALA GLY HIS LYS
497	PRO GLY GLY GLY HIS LYS
498	PRO GLY ILE GLY HIS LYS
499	PRO GLY LEU GLY HIS LYS
500	PRO GLY MET GLY HIS LYS
501	PRO GLY PHE GLY HIS LYS
502	PRO GLY PRO GLY HIS LYS
503	PRO GLY TRP GLY HIS LYS
504	PRO GLY VAL GLY HIS LYS
505	PRO ILE ALA GLY HIS LYS
506	PRO ILE GLY GLY HIS LYS
507	PRO ILE ILE GLY HIS LYS
508	PRO ILE LEU GLY HIS LYS
509	PRO ILE MET GLY HIS LYS
510	PRO ILE PHE GLY HIS LYS
511	PRO ILE PRO GLY HIS LYS
512	PRO ILE TRP GLY HIS LYS
513	PRO ILE VAL GLY HIS LYS
514	PRO LEU ALA GLY HIS LYS
515	PRO LEU GLY GLY HIS LYS
516	PRO LEU ILE GLY HIS LYS
517	PRO LEU LEU GLY HIS LYS
518	PRO LEU MET GLY HIS LYS
519	PRO LEU PHE GLY HIS LYS
520	PRO LEU PRO GLY HIS LYS
521	PRO LEU TRP GLY HIS LYS
522	PRO LEU VAL GLY HIS LYS
523	PRO MET ALA GLY HIS LYS
524	PRO MET GLY GLY HIS LYS
525	PRO MET ILE GLY HIS LYS
526	PRO MET LEU GLY HIS LYS
527	PRO MET MET GLY HIS LYS
528	PRO MET PHE GLY HIS LYS
529	PRO MET PRO GLY HIS LYS

530	PRO MET TRP GLY HIS LYS
531	PRO MET VAL GLY HIS LYS
532	PRO PHE ALA GLY HIS LYS
533	PRO PHE GLY GLY HIS LYS
534	PRO PHE ILE GLY HIS LYS
535	PRO PHE LEU GLY HIS LYS
536	PRO PHE MET GLY HIS LYS
537	PRO PHE PHE GLY HIS LYS
538	PRO PHE PRO GLY HIS LYS
539	PRO PHE TRP GLY HIS LYS
540	PRO PHE VAL GLY HIS LYS
541	PRO PRO ALA GLY HIS LYS
542	PRO PRO GLY GLY HIS LYS
543	PRO PRO ILE GLY HIS LYS
544	PRO PRO LEU GLY HIS LYS
545	PRO PRO MET GLY HIS LYS
546	PRO PRO PHE GLY HIS LYS
547	PRO PRO PRO GLY HIS LYS
548	PRO PRO TRP GLY HIS LYS
549	PRO PRO VAL GLY HIS LYS
550	PRO TRP ALA GLY HIS LYS
551	PRO TRP GLY GLY HIS LYS
552	PRO TRP ILE GLY HIS LYS
553	PRO TRP LEU GLY HIS LYS
554	PRO TRP MET GLY HIS LYS
555	PRO TRP PHE GLY HIS LYS
556	PRO TRP PRO GLY HIS LYS
557	PRO TRP TRP GLY HIS LYS
558	PRO TRP VAL GLY HIS LYS
559	PRO VAL ALA GLY HIS LYS
560	PRO VAL GLY GLY HIS LYS
561	PRO VAL ILE GLY HIS LYS
562	PRO VAL LEU GLY HIS LYS
563	PRO VAL MET GLY HIS LYS
564	PRO VAL PHE GLY HIS LYS
565	PRO VAL PRO GLY HIS LYS
566	PRO VAL TRP GLY HIS LYS
567	PRO VAL VAL GLY HIS LYS
568	TRP ALA ALA GLY HIS LYS
569	TRP ALA GLY GLY HIS LYS
570	TRP ALA ILE GLY HIS LYS
571	TRP ALA LEU GLY HIS LYS
572	TRP ALA MET GLY HIS LYS
573	TRP ALA PHE GLY HIS LYS
574	TRP ALA PRO GLY HIS LYS
575	TRP ALA TRP GLY HIS LYS
576	TRP ALA VAL GLY HIS LYS
577	TRP GLY ALA GLY HIS LYS

578	TRP GLY GLY GLY HIS LYS
579	TRP GLY ILE GLY HIS LYS
580	TRP GLY LEU GLY HIS LYS
581	TRP GLY MET GLY HIS LYS
582	TRP GLY PHE GLY HIS LYS
583	TRP GLY PRO GLY HIS LYS
584	TRP GLY TRP GLY HIS LYS
585	TRP GLY VAL GLY HIS LYS
586	TRP ILE ALA GLY HIS LYS
587	TRP ILE GLY GLY HIS LYS
588	TRP ILE ILE GLY HIS LYS
589	TRP ILE LEU GLY HIS LYS
590	TRP ILE MET GLY HIS LYS
591	TRP ILE PHE GLY HIS LYS
592	TRP ILE PRO GLY HIS LYS
593	TRP ILE TRP GLY HIS LYS
594	TRP ILE VAL GLY HIS LYS
595	TRP LEU ALA GLY HIS LYS
596	TRP LEU GLY GLY HIS LYS
597	TRP LEU ILE GLY HIS LYS
598	TRP LEU LEU GLY HIS LYS
599	TRP LEU MET GLY HIS LYS
600	TRP LEU PHE GLY HIS LYS
601	TRP LEU PRO GLY HIS LYS
602	TRP LEU TRP GLY HIS LYS
603	TRP LEU VAL GLY HIS LYS
604	TRP MET ALA GLY HIS LYS
605	TRP MET GLY GLY HIS LYS
606	TRP MET ILE GLY HIS LYS
607	TRP MET LEU GLY HIS LYS
608	TRP MET MET GLY HIS LYS
609	TRP MET PHE GLY HIS LYS
610	TRP MET PRO GLY HIS LYS
611	TRP MET TRP GLY HIS LYS
612	TRP MET VAL GLY HIS LYS
613	TRP PHE ALA GLY HIS LYS
614	TRP PHE GLY GLY HIS LYS
615	TRP PHE ILE GLY HIS LYS
616	TRP PHE LEU GLY HIS LYS
617	TRP PHE MET GLY HIS LYS
618	TRP PHE PHE GLY HIS LYS
619	TRP PHE PRO GLY HIS LYS
620	TRP PHE TRP GLY HIS LYS
621	TRP PHE VAL GLY HIS LYS
622	TRP PRO ALA GLY HIS LYS
623	TRP PRO GLY GLY HIS LYS
624	TRP PRO ILE GLY HIS LYS
625	TRP PRO LEU GLY HIS LYS

626	TRP PRO MET GLY HIS LYS
627	TRP PRO PHE GLY HIS LYS
628	TRP PRO PRO GLY HIS LYS
629	TRP PRO TRP GLY HIS LYS
630	TRP PRO VAL GLY HIS LYS
631	TRP TRP ALA GLY HIS LYS
632	TRP TRP GLY GLY HIS LYS
633	TRP TRP ILE GLY HIS LYS
634	TRP TRP LEU GLY HIS LYS
635	TRP TRP MET GLY HIS LYS
636	TRP TRP PHE GLY HIS LYS
637	TRP TRP PRO GLY HIS LYS
638	TRP TRP TRP GLY HIS LYS
639	TRP TRP VAL GLY HIS LYS
640	TRP VAL ALA GLY HIS LYS
641	TRP VAL GLY GLY HIS LYS
642	TRP VAL ILE GLY HIS LYS
643	TRP VAL LEU GLY HIS LYS
644	TRP VAL MET GLY HIS LYS
645	TRP VAL PHE GLY HIS LYS
646	TRP VAL PRO GLY HIS LYS
647	TRP VAL TRP GLY HIS LYS
648	TRP VAL VAL GLY HIS LYS
649	VAL ALA ALA GLY HIS LYS
650	VAL ALA GLY GLY HIS LYS
651	VAL ALA ILE GLY HIS LYS
652	VAL ALA LEU GLY HIS LYS
653	VAL ALA MET GLY HIS LYS
654	VAL ALA PHE GLY HIS LYS
655	VAL ALA PRO GLY HIS LYS
656	VAL ALA TRP GLY HIS LYS
657	VAL ALA VAL GLY HIS LYS
658	VAL GLY ALA GLY HIS LYS
659	VAL GLY GLY GLY HIS LYS
660	VAL GLY ILE GLY HIS LYS
661	VAL GLY LEU GLY HIS LYS
662	VAL GLY MET GLY HIS LYS
663	VAL GLY PHE GLY HIS LYS
664	VAL GLY PRO GLY HIS LYS
665	VAL GLY TRP GLY HIS LYS
666	VAL GLY VAL GLY HIS LYS
667	VAL ILE ALA GLY HIS LYS
668	VAL ILE GLY GLY HIS LYS
669	VAL ILE ILE GLY HIS LYS
670	VAL ILE LEU GLY HIS LYS
671	VAL ILE MET GLY HIS LYS
672	VAL ILE PHE GLY HIS LYS
673	VAL ILE PRO GLY HIS LYS

674	VAL ILE TRP GLY HIS LYS
675	VAL ILE VAL GLY HIS LYS
676	VAL LEU ALA GLY HIS LYS
677	VAL LEU GLY GLY HIS LYS
678	VAL LEU ILE GLY HIS LYS
679	VAL LEU LEU GLY HIS LYS
680	VAL LEU MET GLY HIS LYS
681	VAL LEU PHE GLY HIS LYS
682	VAL LEU PRO GLY HIS LYS
683	VAL LEU TRP GLY HIS LYS
684	VAL LEU VAL GLY HIS LYS
685	VAL MET ALA GLY HIS LYS
686	VAL MET GLY GLY HIS LYS
687	VAL MET ILE GLY HIS LYS
688	VAL MET LEU GLY HIS LYS
689	VAL MET MET GLY HIS LYS
690	VAL MET PHE GLY HIS LYS
691	VAL MET PRO GLY HIS LYS
692	VAL MET TRP GLY HIS LYS
693	VAL MET VAL GLY HIS LYS
694	VAL PHE ALA GLY HIS LYS
695	VAL PHE GLY GLY HIS LYS
696	VAL PHE ILE GLY HIS LYS
697	VAL PHE LEU GLY HIS LYS
698	VAL PHE MET GLY HIS LYS
699	VAL PHE PHE GLY HIS LYS
700	VAL PHE PRO GLY HIS LYS
701	VAL PHE TRP GLY HIS LYS
702	VAL PHE VAL GLY HIS LYS
703	VAL PRO ALA GLY HIS LYS
704	VAL PRO GLY GLY HIS LYS
705	VAL PRO ILE GLY HIS LYS
706	VAL PRO LEU GLY HIS LYS
707	VAL PRO MET GLY HIS LYS
708	VAL PRO PHE GLY HIS LYS
709	VAL PRO PRO GLY HIS LYS
710	VAL PRO TRP GLY HIS LYS
711	VAL PRO VAL GLY HIS LYS
712	VAL TRP ALA GLY HIS LYS
713	VAL TRP GLY GLY HIS LYS
714	VAL TRP ILE GLY HIS LYS
715	VAL TRP LEU GLY HIS LYS
716	VAL TRP MET GLY HIS LYS
717	VAL TRP PHE GLY HIS LYS
718	VAL TRP PRO GLY HIS LYS
719	VAL TRP TRP GLY HIS LYS
720	VAL TRP VAL GLY HIS LYS
721	VAL VAL ALA GLY HIS LYS

722	VAL VAL GLY GLY HIS LYS
723	VAL VAL ILE GLY HIS LYS
724	VAL VAL LEU GLY HIS LYS
725	VAL VAL MET GLY HIS LYS
726	VAL VAL PHE GLY HIS LYS
727	VAL VAL PRO GLY HIS LYS
728	VAL VAL TRP GLY HIS LYS
729	VAL VAL VAL GLY HIS LYS

In some embodiments, the structural formula of the cyclic peptide compound is as shown in Table B.

Table B: The preferred structural formula of the cyclic peptide compound (all amino acids are of L-configuration)

SEQ ID NO:	The structural formula of the cyclic peptide compound
52	ALA PHE PRO GLY HIS LYS
214	ILE PHE PRO GLY HIS LYS
414	PHE ALA VAL GLY HIS LYS
250	LEU ALA PRO GLY HIS LYS
297	LEU PHE VAL GLY HIS LYS
205	ILE MET PRO GLY HIS LYS
289	LEU PHE ALA GLY HIS LYS
291	LEU PHE ILE GLY HIS LYS
196	ILE LEU PRO GLY HIS LYS
232	ILE TRP PRO GLY HIS LYS
268	LEU ILE PRO GLY HIS LYS
292	LEU PHE LEU GLY HIS LYS
707	VAL PRO MET GLY HIS LYS
340	MET GLY PRO GLY HIS LYS
710	VAL PRO TRP GLY HIS LYS
293	LEU PHE MET GLY HIS LYS
169	ILE ALA PRO GLY HIS LYS
79	ALA VAL PRO GLY HIS LYS
421	PHE GLY PRO GLY HIS LYS
296	LEU PHE TRP GLY HIS LYS
46	ALA PHE ALA GLY HIS LYS
295	LEU PHE PRO GLY HIS LYS
25	ALA ILE PRO GLY HIS LYS
246	LEU ALA ILE GLY HIS LYS
286	LEU MET PRO GLY HIS LYS
304	LEU PRO PRO GLY HIS LYS
252	LEU ALA VAL GLY HIS LYS
277	LEU LEU PRO GLY HIS LYS
380	MET PRO GLY GLY HIS LYS
461	PHE PRO GLY GLY HIS LYS
160	GLY VAL PRO GLY HIS LYS
367	MET MET PRO GLY HIS LYS
358	MET LEU PRO GLY HIS LYS
349	MET ILE PRO GLY HIS LYS
62	ALA PRO TRP GLY HIS LYS

3	ALA ALA ILE GLY HIS LYS
4	ALA ALA LEU GLY HIS LYS
9	ALA ALA VAL GLY HIS LYS
84	GLY ALA ILE GLY HIS LYS
85	GLY ALA LEU GLY HIS LYS
88	GLY ALA PRO GLY HIS LYS
90	GLY ALA VAL GLY HIS LYS
165	ILE ALA ILE GLY HIS LYS
166	ILE ALA LEU GLY HIS LYS
168	ILE ALA PHE GLY HIS LYS
171	ILE ALA VAL GLY HIS LYS
245	LEU ALA GLY GLY HIS LYS
247	LEU ALA LEU GLY HIS LYS
248	LEU ALA MET GLY HIS LYS
249	LEU ALA PHE GLY HIS LYS
251	LEU ALA TRP GLY HIS LYS
325	MET ALA ALA GLY HIS LYS
327	MET ALA ILE GLY HIS LYS
328	MET ALA LEU GLY HIS LYS
331	MET ALA PRO GLY HIS LYS
333	MET ALA VAL GLY HIS LYS
406	PHE ALA ALA GLY HIS LYS
407	PHE ALA GLY GLY HIS LYS
408	PHE ALA ILE GLY HIS LYS
409	PHE ALA LEU GLY HIS LYS
412	PHE ALA PRO GLY HIS LYS
568	TRP ALA ALA GLY HIS LYS
569	TRP ALA GLY GLY HIS LYS
570	TRP ALA ILE GLY HIS LYS
571	TRP ALA LEU GLY HIS LYS
574	TRP ALA PRO GLY HIS LYS
576	TRP ALA VAL GLY HIS LYS
649	VAL ALA ALA GLY HIS LYS
650	VAL ALA GLY GLY HIS LYS
651	VAL ALA ILE GLY HIS LYS
652	VAL ALA LEU GLY HIS LYS
655	VAL ALA PRO GLY HIS LYS
657	VAL ALA VAL GLY HIS LYS

In some embodiments, the structural formula of the cyclic peptide compound is as shown in Table C.

Table C: The more preferred structural formula of the cyclic peptide compound (all amino acids are of L-configuration)

SEQ ID NO:	The structural formula of the cyclic peptide compound
4	ALA ALA LEU GLY HIS LYS
9	ALA ALA VAL GLY HIS LYS
25	ALA ILE PRO GLY HIS LYS
46	ALA PHE ALA GLY HIS LYS
52	ALA PHE PRO GLY HIS LYS

79	ALA VAL PRO GLY HIS LYS
85	GLY ALA LEU GLY HIS LYS
88	GLY ALA PRO GLY HIS LYS
160	GLY VAL PRO GLY HIS LYS
166	ILE ALA LEU GLY HIS LYS
169	ILE ALA PRO GLY HIS LYS
171	ILE ALA VAL GLY HIS LYS
196	ILE LEU PRO GLY HIS LYS
205	ILE MET PRO GLY HIS LYS
214	ILE PHE PRO GLY HIS LYS
232	ILE TRP PRO GLY HIS LYS
245	LEU ALA GLY GLY HIS LYS
246	LEU ALA ILE GLY HIS LYS
247	LEU ALA LEU GLY HIS LYS
249	LEU ALA PHE GLY HIS LYS
250	LEU ALA PRO GLY HIS LYS
252	LEU ALA VAL GLY HIS LYS
268	LEU ILE PRO GLY HIS LYS
286	LEU MET PRO GLY HIS LYS
289	LEU PHE ALA GLY HIS LYS
291	LEU PHE ILE GLY HIS LYS
292	LEU PHE LEU GLY HIS LYS
293	LEU PHE MET GLY HIS LYS
295	LEU PHE PRO GLY HIS LYS
296	LEU PHE TRP GLY HIS LYS
297	LEU PHE VAL GLY HIS LYS
304	LEU PRO PRO GLY HIS LYS
340	MET GLY PRO GLY HIS LYS
380	MET PRO GLY GLY HIS LYS
406	PHE ALA ALA GLY HIS LYS
409	PHE ALA LEU GLY HIS LYS
412	PHE ALA PRO GLY HIS LYS
414	PHE ALA VAL GLY HIS LYS
421	PHE GLY PRO GLY HIS LYS
461	PHE PRO GLY GLY HIS LYS
568	TRP ALA ALA GLY HIS LYS
574	TRP ALA PRO GLY HIS LYS
576	TRP ALA VAL GLY HIS LYS
649	VAL ALA ALA GLY HIS LYS
650	VAL ALA GLY GLY HIS LYS
652	VAL ALA LEU GLY HIS LYS
655	VAL ALA PRO GLY HIS LYS
707	VAL PRO MET GLY HIS LYS
710	VAL PRO TRP GLY HIS LYS

In some embodiments, the structural formula of the cyclic peptide compound is as shown in Table D.

Table D: The most preferred structural formula of the cyclic peptide compound (all amino acids are of L-configuration)

SEQ ID NO:	The structural formula of the cyclic peptide compound
414	PHE ALA VAL GLY HIS LYS
250	LEU ALA PRO GLY HIS LYS
205	ILE MET PRO GLY HIS LYS
292	LEU PHE LEU GLY HIS LYS
52	ALA PHE PRO GLY HIS LYS
214	ILE PHE PRO GLY HIS LYS
297	LEU PHE VAL GLY HIS LYS
289	LEU PHE ALA GLY HIS LYS
291	LEU PHE ILE GLY HIS LYS
196	ILE LEU PRO GLY HIS LYS
232	ILE TRP PRO GLY HIS LYS
268	LEU ILE PRO GLY HIS LYS
707	VAL PRO MET GLY HIS LYS
340	MET GLY PRO GLY HIS LYS
710	VAL PRO TRP GLY HIS LYS

The amino acid on the left side and the amino acid on the right side form a loop via a peptide bond in the structural formula of the cyclic peptide compound shown in Table A, Table B, Table C, and Table D.

In a second aspect of the invention, the present invention provides a pharmaceutical composition comprising the cyclic peptide compound or the stereoisomer thereof as previously described.

In some embodiments, the pharmaceutical composition further comprises at least one carrier and/or excipient.

In a third aspect of the invention, the present invention provides a cosmetic composition (such as a skin care product, a cosmetic, a hair growth solution, etc.) comprising the cyclic peptide compound or the stereoisomer thereof as previously described.

In some embodiments, the cosmetic composition further comprises a functional substance.

In some embodiments, the functional substance is one or more selected from the group consisting of skin conditioning agents, antioxidants, surfactants, humectants, preservatives, chelating agents, and flavor essences.

In a fourth aspect of the invention, the present invention provides use of the cyclic peptide compound or the stereoisomer thereof as previously described or the pharmaceutical composition as previously described in the manufacture of a medicament which is used for one or more selected from the following (1) - (7):

- (1) delaying skin aging;
- (2) reducing skin damage;
- (3) accelerating skin wound healing;
- (4) reducing hyperpigmentation;
- (5) stimulating hair growth;
- (6) improving the success rate of hair transplantation;
- (7) preventing hair loss.

In a fifth aspect of the invention, the present invention provides the cyclic peptide compound or the stereoisomer thereof as previously described or the pharmaceutical composition as previously described for use in one or more uses selected from the following (1) - (7):

- (1) delaying skin aging;

- (2) reducing skin damage;
- (3) accelerating skin wound healing;
- (4) reducing hyperpigmentation;
- (5) stimulating hair growth;
- 5 (6) improving the success rate of hair transplantation;
- (7) preventing hair loss.

In a sixth aspect of the invention, the present invention provides a method selected from one or more of the following (1) - (7), the method comprising: administering to a subject in need thereof an effective amount of the cyclic peptide compound or the stereoisomer thereof as previously described or the pharmaceutical composition as previously described,

- (1) a method for delaying skin aging;
- (2) a method for reducing skin damage;
- (3) a method for accelerating skin wound healing;
- 15 (4) a method for reducing hyperpigmentation;
- (5) a method for stimulating hair growth;
- (6) a method for improving the success rate of hair transplantation;
- (7) a method for preventing hair loss.

In a seventh aspect of the invention, the present invention provides use of the cyclic peptide compound or the stereoisomer thereof as previously described or the cosmetic composition as previously described in one or more selected from the following (1) - (17), wherein the use is a non-therapeutic use,

- (1) anti-aging of the skin;
- (2) anti-wrinkling of the skin and reducing fine lines;
- 25 (3) improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;
- (4) increasing skin density (reconstitution effect);
- (5) increasing skin volume (abundance effect);
- (6) combating the appearance of stretch marks;
- 30 (7) reducing skin damage;
- (8) accelerating skin wound healing;
- (9) anti-spot;
- (10) improving skin homogeneity and/or luster;
- (11) reducing skin pigmentation;
- 35 (12) moisturizing;
- (13) stimulating hair growth;
- (14) improving the success rate of hair transplantation;
- (15) preventing hair loss;
- (16) topical cosmetology of eyelashes;
- 40 (17) increasing hair width, density, and/or length.

In an eighth aspect of the invention, the present invention provides a method selected from one or more of the following (1) - (17), the method comprising: administering to a subject in need thereof an effective amount of the cyclic peptide compound or the stereoisomer thereof as previously described or a cosmetic composition as previously described,

- (1) a method for anti-aging of the skin;
- (2) a method for anti-wrinkling of the skin and reducing fine lines;
- (3) a method for improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;
- 50 (4) a method for increasing skin density (reconstitution effect);

- (5) a method for increasing skin volume (abundance effect);
 - (6) a method for combating the appearance of stretch marks;
 - (7) a method for reducing skin damage;
 - (8) a method for accelerating skin wound healing;
 - 5 (9) a method for anti-spot;
 - (10) a method for improving skin homogeneity and/or luster;
 - (11) a method for reducing skin pigmentation;
 - (12) a method for moisturizing;
 - (13) a method for stimulating hair growth;
 - 10 (14) a method for improving the success rate of hair transplantation;
 - (15) a method for preventing hair loss;
 - (16) a method for topical cosmetology of eyelashes;
 - (17) a method for increasing hair width, density, and/or length.
- In a ninth aspect of the invention, the present invention provides use of the
- 15 cyclic peptide compound or the stereoisomer thereof as previously described or the cosmetic composition as previously described in one or more selected from the following (1) - (17):
- (1) anti-aging of the skin;
 - (2) anti-wrinkling of the skin and reducing fine lines;
 - 20 (3) improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;
 - (4) increasing skin density (reconstitution effect);
 - (5) increasing skin volume (abundance effect);
 - (6) combating the appearance of stretch marks;
 - 25 (7) reducing skin damage;
 - (8) accelerating skin wound healing;
 - (9) anti-spot;
 - (10) improving skin homogeneity and/or luster;
 - (11) reducing skin pigmentation;
 - 30 (12) moisturizing;
 - (13) stimulating hair growth;
 - (14) improving the success rate of hair transplantation;
 - (15) preventing hair loss;
 - (16) topical cosmetology of eyelashes;
 - 35 (17) increasing hair width, density, and/or length.

Beneficial Effects

1. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof can achieve anti-wrinkling efficacy by significantly increasing Collagen I content.
- 40 2. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof can significantly increase hyaluronic acid (HA) content, thereby achieving compactness efficacy.
- 45 3. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof can significantly increase elastin content, thereby achieving compactness efficacy.

4. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof can significantly increase the Collagen I content, the hyaluronic acid (HA) content and the elastin content, thereby achieving anti-wrinkling efficacy and compactness efficacy with excellent medical and cosmetic effects.

5. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) does not exhibit significant cytotoxicity (e.g. within the concentration range of 5 μ M) and has a good prospect for pharmaceutical and cosmetic applications.

6. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof, when used as a medicament, has one or more beneficial effects selected from the following:

- (1) delaying skin aging;
- (2) reducing skin damage;
- (3) accelerating skin wound healing;
- (4) reducing hyperpigmentation;
- (5) stimulating hair growth;
- (6) improving the success rate of hair transplantation;
- (7) preventing hair loss.

7. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof, when used as a cosmetic for a non-therapeutic use, has one or more beneficial effects selected from the following:

- (1) anti-aging of the skin;
- (2) anti-wrinkling of the skin and reducing fine lines;
- (3) improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;
- (4) increasing skin density (reconstitution effect);
- (5) increasing skin volume (abundance effect);
- (6) combating the appearance of stretch marks;
- (7) reducing skin damage;
- (8) accelerating skin wound healing;
- (9) anti-spot;
- (10) improving skin homogeneity and/or luster;
- (11) reducing skin pigmentation;
- (12) moisturizing;
- (13) stimulating hair growth;
- (14) improving the success rate of hair transplantation;
- (15) preventing hair loss;
- (16) topical cosmetology of eyelashes;
- (17) increasing hair width, density, and/or length.

8. The cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof, when used as a cosmetic, has one or more beneficial effects selected from the following:

- (1) anti-aging of the skin;
- (2) anti-wrinkling of the skin and reducing fine lines;
- (3) improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;

- (4) increasing skin density (reconstitution effect);
(5) increasing skin volume (abundance effect);
(6) combating the appearance of stretch marks;
(7) reducing skin damage;
5 (8) accelerating skin wound healing;
(9) anti-spot;
(10) improving skin homogeneity and/or luster;
(11) reducing skin pigmentation;
(12) moisturizing;
10 (13) stimulating hair growth;
(14) improving the success rate of hair transplantation;
(15) preventing hair loss;
(16) topical cosmetology of eyelashes;
(17) increasing hair width, density, and/or length.
15 9. The efficacy of the cyclic peptide compound of the present invention (e.g., the cyclic peptide compound in Table A, Table B, Table C, or Table D) or the stereoisomer thereof in the above eight aspects are comparable to or even better than that of GHK tripeptide.

20 DETAILED DESCRIPTION OF EMBODIMENTS

Embodiments of the present invention will be described in detail below with reference to examples; however, those skilled in the art will understand that the following examples are only used to illustrate the present invention and should not be regarded as limiting the scope of the present invention. If no specific conditions
25 are specified in the examples, experiments are carried out according to conventional conditions or conditions recommended by the manufacturer. If manufacturers of reagents or instruments used are not specified, the reagents or instruments are conventional products commercially available.

In the present invention, scientific and technical terms used herein have the meanings commonly understood by those skilled in the art unless otherwise
30 indicated. Moreover, the terms and laboratory procedures as used herein related to the chemistry of proteins and nucleic acids, molecular biology, cell and tissue culture, microbiology, and immunology are commonly used terms and routine procedures in their respective fields. At the same time, for a better understanding of the present
35 invention, definitions and explanations of relevant terms are provided below.

The term “stereoisomer” means that in a compound molecule of the same formula, atoms or substituents are linked to each other in the same order, but are in different spatial arrangements, belonging to an isomerism in organic chemistry.

The term “absent” means that the groups on both sides are directly linked. For
40 example, if AA4 is absent in a cyclic peptide compound represented by formula I, the structural formula of the cyclic peptide compound represented by the formula I has become *AA1-AA2-GLY-HIS-LYS-AA3*.

The term “carrier” refers to a system that can alter the way a drug enters a person’s body and distribute the drug in the body, control the release rate of the drug,
45 and deliver the drug to the targeted organ. Drug carrier release and targeting systems can reduce drug degradation and loss, reduce side effects, and improve bioavailability. The macromolecular surfactants that can be used as carriers, due to their unique amphiphilic structure, can be self-assembled, forming various forms of aggregates, such as micelles, microemulsions, gels, liquid crystals, vesicles, etc., as
50 preferred examples. These aggregates have the ability to encapsulate and load drug

molecules and at the same time have good permeability to membranes, which can serve as excellent drug carriers.

The term “excipient” refers to an additive in a pharmaceutical formulation other than the main drug, which may also be referred to as an auxiliary material. The auxiliary material includes, but is not limited to: an ion exchanger, alumina, aluminum stearate, lecithin, serum proteins such as albumin prepared from human plasma, buffer substances such as phosphate, glycerol, sorbic acid, potassium sorbate, a mixture of partial glycerides of saturated vegetable fatty acids, water, salts or electrolytes such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinylpyrrolidone, cellulose substances, polyethylene glycols, sodium carboxymethyl cellulose, polyacrylates, bee wax, and lanolin.

The term “skin conditioning agent” includes, but is not limited to, hydroquinone, kojic acid, arbutin, ellagic acid, azelaic acid, azelaionyldiglycine, L-ascorbic acid and derivatives thereof, licorice extract, *Malpighia emarginata* fruit extract, *Hydrangea macrophylla* extract, alkoxysalicylic acid, *Polygonum cuspidatum* extract, *Sophora japonica* flower extract, turmeric extract, mulberry bark extract, *Phyllanthus emblica* extract, Pea extract, aloin, etc.

The term “antioxidant” includes, but is not limited to, butylated hydroxytoluene, butylated hydroxyanisole, propyl gallate, octyl gallate, dodecanol gallate, tert-butyl hydroquinone, tocopherol, ascorbyl palmitate, isopropyl citrate (mixture), monoglyceride citrate, anoxomer, sodium sulfite, sodium bisulfite, sodium pyrosulfite, cysteine, erythorbic acid, thiourea, dilauryl thiomalonate, nordihydroguaiaretic acid, thioctic acid, alpha-tocopheryl acetate, carotenoids, *Phyllanthus emblica* tannin, ascorbic acid, glutathione, coenzyme Q10, etc.

The term “surfactant” may be an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, a natural surfactant, a fluorine-containing surfactant, etc.

The term “humectant” includes, but is not limited to, glycerol, propylene glycol, butylene glycol, sorbitol, Sorbeth-20, amide humectants, glyceropolyether humectants, lactic acid and sodium lactate, sodium pyrrolidone carboxylate, hydroxyethyl urea, erythritol, glyceropolyether-5 lactate, sodium hyaluronate, saccharide isomers, D-panthenol, polyethylene glycol, diglycerol, methacryloyloxyethyl phosphorylcholine, etc.

The term “preservative” includes, but is not limited to, parabens and salts thereof, formaldehyde and formaldehyde donors, isothiazolinones, phenol preservatives, acid preservatives, halide preservatives, quaternary ammonium compounds, alcohols, commonly used compound preservatives and natural preservatives.

The term “chelating agent” can be selected from ethylenediaminetetraacetic acid and its sodium salt, glycine, citric acid, succinic acid, etc.

The term “flavor essence” may in particular be sandalwood flavor essence, jasmine flavor essence, rose flavor essence, sweet orange flavor essence, or vanilla flavor essence, etc. The flavor essence may also include essential oils, in particular may be sour orange peel oil, bitter orange leaf/shoot oil, geranium oil, *Rosa damascena* flower oil, etc.

The term “treatment” generally refers to obtaining the desired pharmacological and/or physiological effects. The effect may be prophylactic on the basis of the complete or partial prevention of a disease or symptoms thereof; and/or the effect may be therapeutic on the basis of the partial or complete stabilization or cure of the

disease and/or side effects due to the disease. As used herein, "treatment" covers any treatment of a disease in a patient, including: (a) prevention of a disease or symptom in a patient who is susceptible to the disease or symptom but has not been diagnosed with the disease; (b) suppressing a symptom of a disease, i.e., preventing the development thereof; or (c) relieving a symptom of a disease, i.e., causing the disease or symptom to resolve.

The term "subject" includes humans or non-human animals. In the present invention, the term "non-human animals" include all vertebrates, such as non-mammals (e.g., birds, amphibians, reptiles) and mammals such as non-human primates, livestock and/or domesticated animals (e.g., sheep, dogs, cats, cows, pigs, etc.).

The term "an effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve a desired effect. The "effective amount" of the present invention may vary depending on factors such as the individual's skin/hair state, age, sex, and body weight.

In the present invention, 20 conventional amino acids and their abbreviations follow the conventional usage. See Immunology-A Synthesis (the 2nd ed., E.S. Golub and D.R. Gren, Eds., Sinauer Associates, Sunderland, Mass. (1991), which is incorporated herein by reference.

As is well known to those skilled in the art, the term "amino acid residue" refers to the incomplete amino acid structure with an amino terminus (N-terminus) and a carboxy terminus (C-terminus) remained after an amino acid loses one hydrogen on its amino group and one hydroxyl group on its carboxyl group.

In the cyclic peptide compounds of the invention (including but not limited to the cyclic peptide compounds in Table A, Table B, Table C, and Table D), from left to right means from N-terminus to C-terminus by default, and the N-terminus on the left side is connected to C-terminus on the right side to form an NC cyclic peptide, unless otherwise specified.

In addition, the abbreviations in the examples have conventional meanings well known in the art, and are listed below by the way of illustration:

AcOH, Acetic Acid

ACN, Acetonitrile

DCM, Dichloromethane (methylene chloride)

DMF, N,N-Dimethylformamide

DIEA, N,N-Diisopropylethylamine

Fmoc, 9-fluorenylmethyloxycarbonyl

HOBT, 1-Hydroxybenzotriazole

Piperidine, piperidine

PyBOP, Benzotriazol-1-yl-oxytripyrrolidinophosphonium

hexafluorophosphate

Resin, resin

TBTU, O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate

TFA, Trifluoroacetic acid

TFE, 2,2,2-Trifluoroethanol

TIS, Triisopropylsilane

The present invention will be further explained below in connection with specific examples, which are in no way to be construed as limiting the present invention. In addition, raw materials or reagents can be commercially available unless otherwise stated.

Example 1: Synthesis and Identification of Cyclic Peptide Compounds

1. Synthesis of the Cyclic Peptide Compounds

Taking the cyclic peptide compound as set forth in SEQ ID NO: 52 as an example, condensation of the amino acids from C-terminus to N-terminus (from right to left) was performed sequentially by starting with lysine.

5 Step I. Solid-phase synthesis

Fmoc-Lys(Boc)-2-Cl Resin ($S = 0.32 \text{ mmol/g}$) was weighed, placed in a glass reaction column, and swollen with DCM for 30 min. The DCM was removed under reduced pressure. 20% piperidine/DMF solution was added to react for 20 min so as to remove the protecting group Fmoc. The solution was removed under reduced
10 pressure. The resin was washed with DMF five times. Sampling and colour development test were performed. A solid-phase resin with Lys attached (via attachment to the C-terminus of Lys) was obtained.

Fmoc-His(Trt)-OH was weighed and added into the resin, and dissolved with DMF. DIEA and TBTU were added, and the mixture was stirred for 60 min. The
15 solution was removed under reduced pressure. The resin was washed with DMF five times. Sampling and colour development test were performed. A solid-phase resin with Lys-His attached (from C-terminus to N-terminus) was obtained.

The process similar to that described above was repeated. Gly, Pro, Phe, and Ala were sequentially coupled. A solid-phase resin with the polypeptide Lys-His-Gly-Pro-Phe-Ala attached (from C-terminus to N-terminus) was finally obtained,
20 i.e., the peptide resin.

Then, the resin was sequentially washed with DMF, DCM, and methanol three times, and was dried to constant weight.

25 Step II. Cleavage of the peptide resin

Preparation of cleavage reagent: Based on a ratio of 1 g of the peptide resin to 10 mL $\pm$ 2 mL of cleavage reagents ($\text{AcOH} : \text{TFE} : \text{DCM} = 1 : 2 : 7$, volume ratio), the usage amounts of the cleavage reagents were calculated. The specific steps were as follows: the desired cleavage reagents DCM, TFE and AcOH were sequentially
30 added to a cleavage reaction flask, and the temperature of the cleavage reagents were controlled between 0-10°C; the cleavage reagents were added to the peptide resin with stirring, and the temperature of the system was allowed to be stabilized; after the reaction was stirred at a controlled temperature of 25-30°C for 2 hours, the cleavage solution was filtered off.

35 Step III. Dealing with the reaction

The cleavage solution obtained in the Step II was put into a TBTU/DIEA stirring reaction. After the reaction was completed, the solvent was evaporated off on a rotary evaporator. Then, based on a ratio of 1 g of the peptide resin to 10 ml $\pm$ 2 ml of the reagents to be mixed ($\text{TFA} : \text{H}_2\text{O} : \text{TIS} = 95 : 2.5 : 2.5$, volume ratio), the usage amounts of the reagents to be mixed were calculated. Afterwards, the
40 desired reagents H_2O , TFA, and TIS were sequentially added to the reaction flask. After the reaction was stirred for 2 hours, the product was precipitated with ice-cold diethyl ether in an amount 5 times the volume of the concentrated solution. The precipitate was filtered out and was dried under reduced pressure at room temperature to give a crude product.

45 Step IV. Lyophilization and purification

The crude product was ground into a fine powder. Purified water was prepared, and the ground crude product was added slowly with stirring. An acetonitrile-water solution was added dropwise simultaneously. After the addition and dissolution of the crude product were completed, the solution was filtered through a 0.45 μm
50 microporous filter membrane. The crude product was purified using a C-18 packing

preparative column. Mobile phase A was 0.1% TFA in water; and mobile phase B was 0.1% TFA in acetonitrile. Separation and purification were performed at ambient temperature with an appropriate gradient. The target products were collected, analyzed and detected, and classified. The purity requirement was $\geq 95\%$.

- 5 Unqualified target product was collected and further separated and purified using an appropriate gradient. The qualified main peak was freeze-dried under reduced pressure to give the refined polypeptide (SEQ ID NO: 52) in a powder form.

Other cyclic peptide compounds of the present application can be prepared by those skilled in the art by reference to the synthesis procedures described above.

10 2. Identification of the Cyclic Peptide Compounds

The refined polypeptide prepared above was weighed, dissolved in a mixed solution of water and acetonitrile until the solution became clear, filtered and then loaded for detection. Detection conditions of high performance liquid chromatography: C18 column, $4.6\ \mu\text{m} \times 250\ \text{mm}$; mobile phase A: 0.1% TFA in acetonitrile, mobile phase B: 0.1% TFA in water; gradient conditions: 25% A and 75% B at 0.01 min $\rightarrow$ 50% A and 50% B at 25 min $\rightarrow$ 100% A at 25.01 min $\rightarrow$ stop at 30 min; detection wavelength: 220 nm; flow rate: 1.0 ml/min; column temperature: 25°C; injection volume: 10 μL .

The detector for mass spectrometry was Agilent-6125B, using an electrospray ion source (ESI), with positive ion scanning; the voltage of mass spectrometry: +4.5 kv; the voltage of detector : 1.5 kv; the flow rate of sprayer: 1.5 L/min; CDL: -20.0 v; CDL temperature: 250°C; heating module temperature: 200°C; mobile phase: 50% water/50% acetonitrile; the flow rate of mobile phase: 0.2 mL/min.

Mass spectral data of some of the exemplary cyclic peptide compounds are shown in Table 1 below.

Table 1: Mass spectral data of the exemplary cyclic peptide compounds

SEQ ID NO:	Theoretical MS value [M+H] ⁺	Measured MS value [M+H] ⁺
52	638.7	639.0
214	680.8	680.8
414	640.8	640.6
250	604.7	604.8
297	682.8	682.8
205	664.8	665.0
289	654.8	654.4
291	696.9	697.0
196	646.8	646.3
232	719.9	719.4
268	646.8	646.5
292	696.9	696.5
707	650.8	650.5
340	608.7	608.4
710	705.8	705.4

As shown in Table 1, the desired cyclic peptide compounds can be successfully obtained by the preparation method of the present invention.

Example 2: Biological Activity Test of the Cyclic Peptide Compounds

30 1. Test Methods

A. Fibroblast cytotoxicity test

Test materials: Fibroblasts of human origin (Guangdong Boxi Biotechnology Co., Ltd., Lot No. Fb20081902), DMEM culture medium (Gibco, 23042301, expiration date on 230522), PBS (Solarbio, P1010), MTT (Sigma, M5655), DMSO (Sigma, D4540-1L), CO₂ incubator (Thermo, 150I), super-clean bench (AIRTECH, SW-CJ-1F), inverted microscope (Olympus, CKX53).

Test methods:

1) Cell inoculation: After cell resuscitation, the cells were inoculated into 96-well plates when the plating rate reached around 60%, and were incubated overnight in an incubator (37°C, 5% CO₂).

2) Test grouping: The blank group, solvent control group, positive control group, and sample group were set for the test. In the sample group, 7 concentration gradients were set for each sample and 3 duplicate wells were set for each concentration gradient.

3) Formulation of solutions: Sample working solutions at different concentrations were formulated based on the test concentrations of 0.0781 μM, 0.1563 μM, 0.3125 μM, 0.625 μM, 1.25 μM, 2.5 μM, and 5 μM.

4) Administration: Administration was performed when the cell plating rate in the 96-well plates reached 50% to 60%. 200 μL of culture medium per well was added for the solvent control group; 200 μL of culture medium containing 10% DMSO per well was added for the positive control group; 200 μL of culture medium containing the sample at a corresponding concentration per well was added for the sample group; The blank group had no cell inoculation, for which only 200 μL of cell culture medium was added. After the administration was complete, the 96-well plates were incubated in an incubator (37°C, 5% CO₂) for 24 h.

5) Detection: After 24 h of cell incubation and culture, the supernatant was discarded, and MTT working solution (0.5 mg/mL) was added. Incubation was performed at 37°C for 4 h in the dark. After the incubation was completed, the supernatant was discarded and 150 μL DMSO was added to each well. The OD value was read at 490 nm.

6) Calculation of relative viability of cells: Calculation was performed according to the formula below:

$$\text{Relative viability of cells} = \frac{\text{Sample well OD} - \text{Blank well OD}}{\text{Solvent control well OD} - \text{Blank well OD}} \times 100\%.$$

The detection results of some of the exemplary cyclic peptide compounds are shown in Table 2.

Table 2: The detection results of the exemplary cyclic peptide compounds

	SE Q ID NO:	Concentration (μM)							Positive control 10% DMSO
		0.0781	0.1563	0.3125	0.625	1.25	2.5	5	
Cyclic peptide compound s	52	96.35%	96.02%	96.69%	96.69%	96.08%	94.03%	93.26%	0.61%
	214	99.39%	98.67%	98.40%	98.67%	97.51%	97.51%	95.36%	0.61%
	414	106.03 %	105.69 %	105.11 %	104.20 %	104.20 %	102.07 %	101.55 %	2.07%
	250	118.62 %	117.01 %	116.72 %	114.43 %	114.02 %	114.60 %	114.89 %	2.07%
	297	103.91 %	102.94 %	102.84 %	102.78 %	101.66 %	100.59 %	100.11 %	0.54%
	205	104.12 %	104.87 %	102.41 %	102.03 %	99.95%	99.41%	99.14%	0.54%
	289	98.48%	96.48%	95.25%	95.39%	95.91%	95.01%	94.87%	0.43%
	291	97.96%	97.15%	97.48%	97.05%	96.58%	94.20%	94.49%	0.43%
	196	101.92 %	101.21 %	102.58 %	101.26 %	100.40 %	101.47 %	99.85%	0.30%

	232	100.44 %	97.64%	93.46%	94.05%	93.90%	91.59%	91.10%	1.87%
	268	97.22%	93.85%	94.77%	91.67%	91.81%	90.66%	90.38%	1.62%
	292	107.68 %	107.63 %	105.05 %	102.37 %	102.07 %	102.88 %	102.88 %	0.30%
	707	102.27 %	98.38%	97.64%	97.83%	93.62%	92.78%	91.58%	1.62%
	340	98.04%	98.71%	97.29%	96.66%	94.99%	94.28%	91.65%	1.17%
	710	97.66%	97.91%	97.54%	96.66%	96.20%	95.37%	95.82%	0.61%

As shown in Table 2, in the fibroblast toxicity test experiment, none of the cyclic peptide compounds exhibited significant cytotoxicity within the concentration range of 5 μ M, with good prospect for pharmaceutical and cosmetic applications.

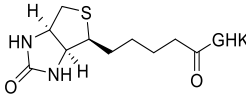
5 B. Collagen I (type I collagen) elevation effect in fibroblasts, hyaluronic acid (HA) elevation effect in fibroblasts, and elastin (ELN) elevation effect in fibroblasts

Test materials: Fibroblasts of human origin (Guangdong Boxi Biotechnology Co., Ltd., Lot No. Fb20081902), DMEM culture medium (Gibco, 23042301, expiration date 230522), PBS (Solarbio, P1010), TGF- β 1 (Peprotech, 230504),
10 Collagen I ELISA Kit (Cusabio, B21025824), Elastin ELISA kit (Abcam, GR3446070-2), HA ELISA kit (RD, P325066). CO₂ incubator (Thermo, 150I), super-clean bench (AIRTECH, SW-CJ-1F), microplate reader (BioTek, Epoch).

Test methods:

1) Inoculation: After cell resuscitation, the cells were inoculated into 6-well plates when the plating rate reached around 60%, and were incubated overnight in
15 an incubator (37°C, 5% CO₂).

2) Formulation of solutions: The cyclic peptide compounds in the sample group,

PC2 (Biotinoyl-GHK, ) and PC3 () in
the positive reference group were all at the concentration of 1 μ M, and the test
substance working solutions were formulated. Only the cell culture medium was
20 added for the blank control group (BC).

3) Administration: When the cell plating rate in the 6-well plates reached 40% to 60%, administration was performed at 2 mL per well. 3 duplicate wells were set for each group. Incubation was performed in an incubator (37°C, 5% CO₂) for 24 h.

4) ELISA assay: The ELISA assay was performed according to the instructions
25 of the ELISA kit, with the detection indicators being Collagen I elevation effect in the fibroblasts, HA elevation effect in the fibroblasts, and elastin elevation effect in the fibroblasts.

The activity test data of some of the exemplary cyclic peptide compounds are shown in Table 3A, Table 3B, and Table 3C below.

30 Table 3A: Data of the Collagen I elevation effect in the fibroblasts for some of the exemplary cyclic peptide compounds

Blank control/SEQ ID NO:	Collagen I elevation effect in the fibroblasts
Blank control (BC)	35.6
414	40.54
250	55.85
205	49.25
214	42.51
297	52.28
289	41
232	67.93

268	61.46
707	66.21
340	90.07
710	110.87

As shown in Table 3A, compared to the BC, the exemplary cyclic peptide compounds of the present invention, such as the cyclic peptide compounds as set forth in SEQ ID NOs: 214, 414, 250, 297, 205, 289, 232, 268, 707, 340, and 710 result in a significant increase in the type I collagen (Collagen I) content, demonstrating that the cyclic peptide compounds of the present invention can achieve **anti-wrinkling efficacy** by increasing the Collagen I content.

Table 3B: Data of the HA elevation effect in the fibroblasts for some of the exemplary cyclic peptide compounds

Blank control/SEQ ID NO:	HA elevation effect in the fibroblasts
Blank control (BC)	1402.44
414	1926.61
250	2142.56
205	2641.21
292	2635.98
52	2900.83
214	1965.3
297	2212.6
289	1978.48
291	2477.91
196	2305.13

As shown in Table 3B, compared to the BC, the exemplary cyclic peptide compounds of the present invention, such as the cyclic peptide compounds as set forth in SEQ ID NOs: 52, 250, 297, 205, 291, 196, 292, 414, 214, and 289 result in a significant increase in the hyaluronic acid (HA) content, demonstrating that the cyclic peptide compounds of the present invention can achieve **compactness efficacy** by increasing the HA content.

Table 3C: Data of the elastin elevation effect in the fibroblasts for some of the exemplary cyclic peptide compounds

Blank control/SEQ ID NO:	Elastin elevation effect in the fibroblasts
Blank control (BC)	756.52
414	1124.58
250	1051.64
205	1074.17
292	1278.99
52	1043.27
214	1050.82
297	923.52
289	1034.59
291	1177.19
196	1175.6
232	1001.84
340	1304.87
710	1207.29

As shown in Table 3C, compared to the BC, the exemplary cyclic peptide compounds of the present invention, such as the cyclic peptide compounds as set forth in SEQ ID NOs: 52, 250, 297, 205, 291, 196, 292, 414, 214, 289, 232, 340, and 710 result in a significant increase in the elastin content, demonstrating that the cyclic peptide compounds of the present invention can achieve **compactness efficacy** by increasing the elastin content.

In addition, as shown in Table 3A, Table 3B, and Table 3C, compared to the BC, the exemplary cyclic peptide compounds of the present invention, such as the cyclic peptide compounds as set forth in SEQ ID NOs: 414, 250, 205, and 292, result in a significant increase in the type I collagen (Collagen I) content, the hyaluronic acid (HA) content, the elastin content, demonstrating that the cyclic peptide compounds of the present invention can achieve the **compactness efficacy and anti-wrinkling efficacy** by increasing the Collagen I content, the HA content and the elastin content, with excellent medical and cosmetic effects.

CLAIMS

1. A cyclic peptide compound represented by formula I, or a stereoisomer thereof,

AA1-AA2-GLY-HIS-LYS-AA4-AA3

Formula I

characterized in that:

AA1 is an amino acid residue:

AA2 is absent or is an amino acid residue;

AA3 is an amino acid residue:

AA4 is absent or is an amino acid residue;

* indicates that the N-terminus and the C-terminus of formula I are linked to form a cyclic peptide;

the amino acid is a natural amino acid or a non-natural amino acid;

the amino acid is of D-configuration or L-configuration, preferably of L-configuration.

2. The cyclic peptide compound or the stereoisomer thereof of claim 1, characterized in that the amino acid is a natural amino acid;

preferably, the amino acid is a hydrophobic natural amino acid;

more preferably, the amino acid is selected from the group consisting of alanine, glycine, isoleucine, leucine, methionine, phenylalanine, proline, tryptophan, and valine.

3. The cyclic peptide compound or the stereoisomer thereof of claim 1 or 2, characterized in that AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

preferably, AA1 is selected from the group consisting of an alanine residue, a methionine residue, a phenylalanine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a glycine residue;

more preferably, AA1 is selected from the group consisting of a methionine residue, an alanine residue, a phenylalanine residue, a glycine residue, and a proline residue.

4. The cyclic peptide compound or the stereoisomer thereof of any one of claims 1-3, characterized in that AA2 is an amino acid residue;

preferably, AA2 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue:

preferably, AA2 is selected from the group consisting of a valine residue, a proline residue, a leucine residue, an alanine residue, an isoleucine residue, a methionine residue, and a tryptophan residue;

more preferably, AA2 is selected from the group consisting of a proline residue, a leucine residue, a valine residue, an isoleucine residue, and a tryptophan residue.

5. The cyclic peptide compound or the stereoisomer thereof of any one of claims 1-4, characterized in that AA3 is selected from the group consisting of a

phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

preferably, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a glycine residue, and a valine residue;

preferably, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, an isoleucine residue, and a valine residue;

more preferably, AA3 is selected from the group consisting of an isoleucine residue, a leucine residue, a phenylalanine residue, a methionine residue, and a valine residue.

6. The cyclic peptide compound or the stereoisomer thereof of any one of claims 1-5, characterized in that AA4 is absent.

7. The cyclic peptide compound or the stereoisomer thereof of any one of claims 1-6, characterized in that the cyclic peptide compound has a structure represented by formula I-1,

AA3-AA1-AA2-GLY-HIS-LYS
Formula I-1

wherein:

AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

preferably, AA1 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a glycine residue;

and/or

AA2 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

preferably, AA2 is selected from the group consisting of an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, and a valine residue;

and/or

AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a proline residue, a glycine residue, and a valine residue;

preferably, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, a tryptophan residue, an isoleucine residue, a glycine residue, and a valine residue;

more preferably, AA3 is selected from the group consisting of a phenylalanine residue, an alanine residue, a methionine residue, a leucine residue, an isoleucine residue, and a valine residue;

* indicates that the N-terminus and the C-terminus of the formula I-1 are linked to form a cyclic peptide;

the amino acid is of D-configuration or L-configuration, preferably of L-configuration.

8. The cyclic peptide compound or the stereoisomer thereof of claim 7, characterized in that preferably AA1 is selected from the group consisting of a methionine residue, an alanine residue, a phenylalanine residue, a glycine residue, and a proline residue; and/or
- 5 preferably AA2 is selected from the group consisting of a proline residue, a leucine residue, a valine residue, an isoleucine residue, and a tryptophan residue; and/or
- preferably, AA3 is selected from the group consisting of an isoleucine residue, a leucine residue, a phenylalanine residue, a methionine residue, and a valine residue.
- 10
9. The cyclic peptide compound or the stereoisomer thereof of any one of claims 1-8, characterized in that the structural formula of the cyclic peptide compound is as shown in Table A;
- 15 preferably, the structural formula of the cyclic peptide compound is as shown in Table B;
- more preferably, the structural formula of the cyclic peptide compound is as shown in Table C;
- most preferably, the structural formula of the cyclic peptide compound is as shown in Table D.
- 20
10. A pharmaceutical composition comprising the cyclic peptide compound or the stereoisomer thereof of any one of claims 1-9;
- optionally, further comprising at least one carrier and/or excipient.
- 25
11. A cosmetic composition comprising the cyclic peptide compound or the stereoisomer thereof of any one of claims 1-9;
- optionally, further comprising a functional substance;
- preferably, the functional substance being one or more selected from the group consisting of skin conditioning agents, antioxidants, surfactants, humectants, preservatives, chelating agents, and flavor essences.
- 30
12. Use of the cyclic peptide compound or the stereoisomer thereof of any one of claims 1-9 or the pharmaceutical composition of claim 10 in the manufacture of a medicament which is used for one or more selected from the following (1) - (7):
- 35 (1) delaying skin aging;
- (2) reducing skin damage;
- (3) accelerating skin wound healing;
- (4) reducing hyperpigmentation;
- (5) stimulating hair growth;
- 40 (6) improving the success rate of hair transplantation;
- (7) preventing hair loss.
13. Use of the cyclic peptide compound or the stereoisomer thereof of any one of claims 1-9 or the cosmetic composition of claim 11 in one or more selected from the following (1) - (17):
- 45 (1) anti-aging of the skin;
- (2) anti-wrinkling of the skin and reducing fine lines;
- (3) improving mechanical properties of the skin: firmness, complexion, elasticity, and/or flexibility;
- 50 (4) increasing skin density;

- (5) increasing skin volume;
- (6) combating the appearance of stretch marks;
- (7) reducing skin damage;
- (8) accelerating skin wound healing;
- 5 (9) anti-spot;
- (10) improving skin homogeneity and/or luster;
- (11) reducing skin pigmentation;
- (12) moisturizing;
- (13) stimulating hair growth;
- 10 (14) improving the success rate of hair transplantation;
- (15) preventing hair loss;
- (16) topical cosmetology of eyelashes;
- (17) increasing hair width, density, and/or length.