Design of Functional Foods using Synthetic Conjugates

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Summary. Nutrigenomics can provide a new development of research on functional food and we can create new effective functional foods using the nutrigenomical technique in the future. Many functional compounds to prepare functional foods are construed as a "conjugate" of small chemicals. Thousands of natural conjugates already are known, and we can design and synthesize limitless number of artificial conjugates in addition to them. Conjugates consisting of harmless natural components are expected not only to provide additional new functions but are also harmless. In this review, an idea for designing new functional foods using conjugates and the results of the just launched research based on this idea are shown.

Key words : functional food ; conjugate ; synthesis ; food design

Introduction

Serious rekindling of interest in functional food is one of the recent global trends. In Japan, the Council for Science and Technology Policy takes up "food science and technology" as one of the strategic fields in the science and technology basic plan. The market for "food for specified health use" already has grown over 400 billion-yen-a-year, and the functional food industry is promised future growth. The concept of "functional food" is explained in new foods which contribute to the prevention of disease by modulating the physiological system 1). Most people who desire to become healthier set the trend. On the other side, the health food industry seems to inspire little confidence in the Japanese. To cite an instance, latest opinion polls for business people by UPR Golin/Harris International show that the reliability of the health food industry was next to the last among 25 kinds of major industries. Superficial understanding of functional food should cause this result. Accurate information about functional food must be disseminated to the people through food research. However, in the field of food science, a valuation method for the effectiveness of food is a big issue. The usual food is a mixture of thousands of functional chemicals, and the chemicals show a broad and moderate spectrum by present biological assays. In addition, we have to consider the individual differences in the effectiveness. Therefore, it is difficult to confirm the real effectiveness of food on us. The latest nutritional concept, "nutrigenomics", is expected to break through the issue of food valuation. Nutrigenomics is intended to understand the effects of nutrients in molecular level processes in the body as well as the variable effects nutrients have on each of us as individuals based on regulation of gene expression by food ingestion. During this year, a big project in nutrigenomics research has started in the USA. Nutrigenomics will be a powerful technique for estimating the value of functional food in the near future, and we can create new effective functional foods using the technique. In this review, an idea for designing new functional foods using a conjugate of natural products and the results of the just launched research based on this idea are shown.

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*Studies on Components of Mushroom, Part Ⅹ, For Part Ⅸ see ref. 4.

Conjugates in Nature

Proteins (peptides), polysaccharides, lipids, and glycosides, are major portions of the biological products in nature. These are congeries of each unit compound and are construed as a "conjugate" of them. Usually, a conjugate possesses unique advantages which are lacking in the components, and the separated components play their respective functions. Peptides play an important role in hormonal control in mammals. After playing their role, peptides are digested into amino acids and utilized as components of another hormone and/or body. Several kinds of glycosides keep their stability in water due to the saccharide moieties, and the aglycons exhibit the functions when the saccharide moieties are cleaved. These are smart ways to play many parts using limited items. Though known natural conjugates are limited, combinations of natural compounds are limitless. This shows that we can design and synthesize new types of conjugates in addition to the existent natural conjugates. We already utilize several artificial conjugates consisting of natural compounds.

Research on Conjugates of Natural Compounds

The most popular non-calorie sweetener, aspartame, H-Asp-Phe-OMe can be said to be a conjugate of natural compounds (Fig. 1)[2]. Aspartame was found in the synthetic research on the C-terminal tetrapeptide of gastrin, H-Trp-Met-Asp-Phe-NH_2[3]. H-Asp-OH is one of standard amino acids and H-Phe-OMe is formed from Phe by esterase *in vivo*[4]. Both components exist in nature, but the combination is novel. Each component does not have a sweet taste. Only after forming H-Asp-Phe-OMe does it exhibit a potent sweet taste. The safety of this unique combination of natural products is confirmed.

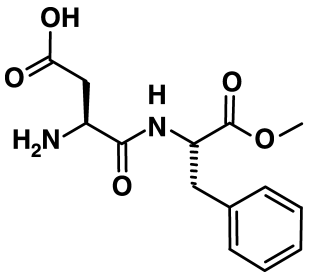


Fig. 1. Aspartame
(H-Asp-Phe-OMe)

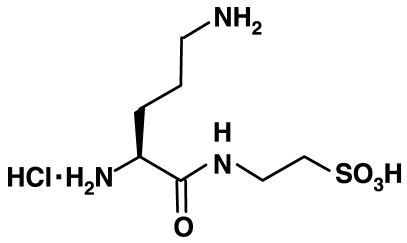


Fig. 2. Ornithyltaurine · hydrochloride

Other researches on artificial conjugate are being conducted. A salty peptide, ornithyltaurine · hydrochloride (Fig. 2)[5], is a novel combination of natural taurine and ornithine. Both components are almost tasteless, but the combination produces a salty taste. This compound was found in researches of structure-taste relationship of slightly salty H-Orn-Gly-OH· HCl, which had been fortuitously found in researches on the structure-bitter taste relationship of N-terminus analogue of BPIa (H-Arg-Gly-Pro-Pro-Phe-Ile-Val-OH) from casein hydrolysis. The salty peptide related analogues are shown in Table 1. Tastes of the peptides are variously changed by the amino acids sequence. The C-terminus amino acid generally has reference to taste of the peptide, and the taste is intensified in the peptide. The N-terminus amino acid is also important to exhibit good taste. The best sequence is ornithyl-taurine, and the salty taste is similar to NaCl. These compounds are expected to be safe because of the harmless nature of the components.

O-Aminoacyl sugar, which have been developed in 1985[6i], is a conjugate of a saccharide and a

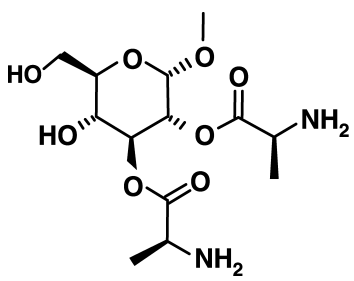


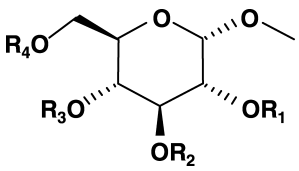
Fig. 3. *O*-Aminocyl Sugar
(methyl 2,3-di-*O*alanyl-α-D-glucopyranoside)

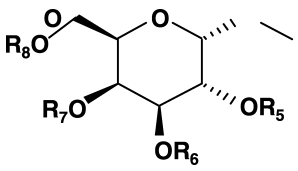
Table 1. Taste Properties of Salty Peptide Amalogues[5d)]

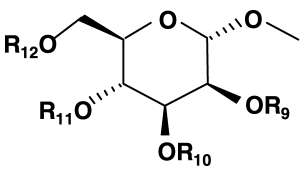
Peptides	Taste	T.V.[a] (mM)	C-A.A.[b]	Taste/T.V.	N-A.A.[c]	Taste/T.V.
Dap-Gly.HCl	umami	2.4	Dap[c]	–	Gly	sweet/38mM[6d]
Dap-β-Ala.HCl	umami	6.3			β-Ala	flat
Dap-GABA.HCl	flat[b)]	2.4			GABA[g]	flat
Dab-Gly.HCl	umami	1.6	Dab[f]	–	Gly	sweet/38mM
Dab-β-Ala.HCl	umami	1.6			β-Ala	flat
Dab-GABA.HCl	salty(weak)	1.6			GABA	flat
Om-Gly.HCl	salty/umami	1.3	Orn[h]	sweet>salty>umami/1%(w/v)	Gly	sweet/38mM
Om-β-Ala.HCl	salty	1.4			β-Ala	flat
Om-GABA.HCl	salty	1.2			GABA	flat
Lys-Gly.HCl	salty/umami	6.3	Lys	bitter>salty>umami/1%(w/v)	Gly	sweet/38mM
Lys-β-Ala.HCl	umami				β-Ala	flat
Lys-GABA.HCl	umami	5.5			GABA	flat
Gly-Om.HCl	sour/sweet	4.8	Gly	sweet/38mM	Orn	sweet>salty>umami/1%(w/v)
β-Ala-Om.HCl	sour/sweet	2.9	β-Ala	flat		
GABA-Om.HCl	sweet/sour	5.5	GABA	flat		
Gly-Lys.HCl	sour/sweet	4.7	Gly	sweet/38mM	Lys	bitter>salty>umami/1%(w/v)
β-Ala-Lys.HCl	sweet/sour	1.6	β-Ala	flat		
GABA-Lys.HCl	sweet/sour	5.5	GABA	flat		
Dap-Tau.HCl	sour/sweet	1.6	Dap	–	Tau	flat
Dab-Tau.HCl	sour/salty	3.7	Dab	–		
Om-Tau.HCl	salty	5.2	Orn	sweet>salty>umami/1%(w/v)		
Lys-Tau.HCl	salty	3.1	Lys	bitter>salty>umami/1%(w/v)		

[a] Threshold value [b] An amino acid on C-terminal of peptide [c] An amino acid on N-terminal of peptide
[d] Flat means almost tasteless [e] α,β-Diaminopropionic acid [f] α, γ-Diaminobutyric acid
[g] γ-Aminobutyric acid [h]Ornithine

Table 2. Taste Properties of *O*-Aminoacyl Sugars







O-Aminoacyl Sugars[a]				Taste	T.V. (mM)	Taste of Peptide[b]	T.V. (mM)	
R_1	R_2	R_3	R_4					
H	H	H	H	sweet	weak			7)
(Methyl-α-D-glucopyranoside)								
G	G	H	H	sweet	2.1	sweet	38	6d)
A	A	H	H	sweet	0.32	sweet	25	6d)
F	F	H	H	bitter	0.05	bitter	19	6d)
D-F[c]	D-F	H	H	bitter	0.12	sweet	2.0	6a)
FF	FF	H	H	bitter	0.003	bitter	1.2	6d)
L	L	H	H	bitter	0.08	bitter	0.05	6a,j)
I	I	H	H	bitter	0.2	bitter	0.04	6a,j)
V	V	H	H	sweet	19	sweet>bitter	–	6d)
VV	VV	H	H	bitter	0.25	umami	–	6d)
VVV	VVV	H	H	bitter	0.10	bitter	4.5	6d)
VVVV	VVVV	H	H	bitter	0.05	bitter	2	6d)

Table 2. Continued

O-Aminoacyl Sugars[a]				Taste	T.V. (mM)	Taste of Peptide[b]	T.V. (mM)	
PPGG	PPGG	H	H	bitter	0.0047	bitter	3.0	6d)
PGPG	PGPG	H	H	bitter	0.0058	bitter	0.3	6d)
PGGP	PGGP	H	H	bitter	0.0029	bitter	0.12	6d)
H	A	H	H	sweet	2.3	sweet	25	6a)
H	H	A	A	bitter	0.68	sweet	25	6a)
A	A	A	H	sweet＞bitter	0.55	sweet	25	6a)
A	A	A	A	sweet	2.3	sweet	25	6a)
H	H	H	A	sweet	0.83	sweet	25	6a)
K	K	K	H	sweet	0.47	bitter＞salty＞umami	1%(w/v)	6b),8)
Orn	Orn	Orn	H	salty	0.47	sweet＞salty＞umami	1%(w/v)	6b),8)
Dab	Dab	Dab	H	umami＞sour＞salty	0.40	–	–	6b)
Dap	Dap	Dap	H	sour＞sweet	0.73	–	–	6b)
Orn	Orn	H	H	umami	0.20	sweet＞salty＞umami	1%(w/v)	6b),8)
GG	GG	H	H	tastless	–	tasteless	–	6d)
AA	AA	H	H	sweet＞bitter	–	sweet	6.0	6d)
GGG	GGG	H	H	tasteless	–	tasteless	–	6d)
AAA	AAA	H	H	tasteless	–	sweet	3.0	6d)
GGGG	GGGG	H	H	tasteless	–	tasteless	–	6d)
AAAA	AAAA	H	H	tasteless	–	tasteless	–	6d)
FFF	FFF	H	H	bitter	0.002	bitter	0.2	6d)
R_5	R_6	R_7	R_8					
H	H	H	H	sweet	weak			7)
(Methyl-α-D-galactopyranoside)								
K	K	K	H	sour＞sweet	0.23	bitter＞salty＞umami	1%(w/v)	6b),8)
Orn	Orn	Orn	H	umami	0.25	sweet＞salty＞umami	1%(w/v)	6b),8)
Dab	Dab	Dab	H	umami＞sour＞salty	0.39	–	–	6b)
Dap	Dap	Dap	H	sour＜sweet	0.61	–	–	6b)
Orn	Orn	Orn	Orn	sour＞umami	0.44	sweet＞salty＞umami	1%(w/v)	6b),8)
R_9	R_{10}	R_{11}	R_{12}					
H	H	H	H	sweet	weak			7)
(Methyl-α-D-mannnopyranoside)								
K	K	K	H	sour＞sweet	0.47	bitter＞salty＞umami	1%(w/v)	6b),8)
Orn	Orn	Orn	H	sour＞umami	0.16	sweet＞salty＞umami	1%(w/v)	6b),8)
Dab	Dab	Dab	H	umami＞sour＞salty	0.23	–	–	6b)
Dap	Dap	Dap	H	sour＞sweet	0.36	–	–	6b)
Orn	Orn	Orn	Orn	sour＞astringency	0.13	sweet＞salty＞umami	1%(w/v)	6b),8)

[a] The one-letter amino acid codes are used for standard amino asids and three-letter amino acid codes are used for non standard amino asids.

[b] Tastes of free peptides introducing as R group(s) on saccharides

[c] D-Phenylalanyl

peptide (an amino acid)[6]. A typical *O*-aminoacyl sugar is shown in Fig. 3. Amino acids can be easily introduced onto hydroxyl groups of a saccharide, and *O*-aminoacyl sugars can have various conformations by the change of the saccharide moiety. So relationships between taste and structure of *O*-aminoacyl sugars have been investigated and the results have been shown as the taste tetrahedron (Fig. 4)[6a]. In those studies, they have succeeded in design *O*-aminoacyl sugars with sweetness, bitterness, umami, and saltiness. Taste properties of *O*-aminoacyl sugars are summarized in Table 2. In general, the taste quality of *O*-aminoacyl sugars relate to the peptide or amino acid moieties and the intensities are emphasized. Occasionally, a different taste from both the peptide and the saccharide moiety is exhibited. In this case, the taste of *O*-aminoacyl sugar is stron-

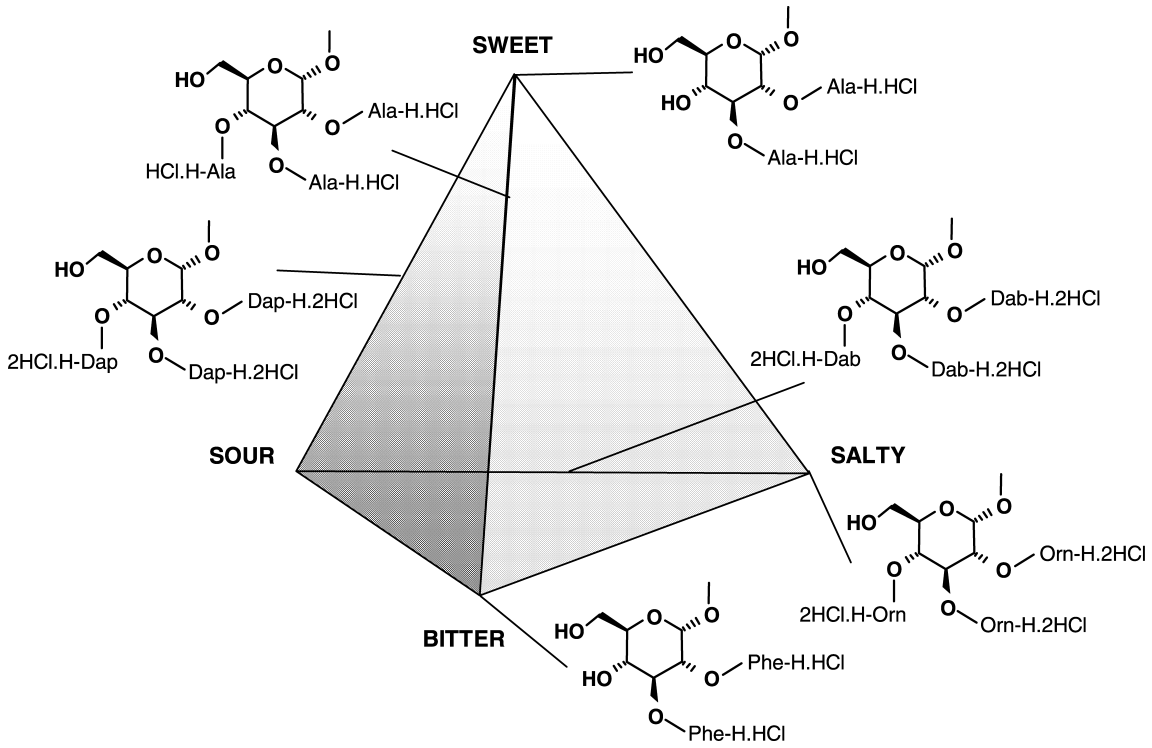


Fig. 4. Taste Tetrahedron with *O*-Aminoacyl Sugars

ger than those of the components. *O*-Aminoacyl sugar is easily digested to the peptide and saccharide moiety by treatment of tripsin or chimotripsin and is expected to be safe.

In 1987, cinnamic acid derivatives consisting of a phenolic acid and an amino acid as angiotensin converting enzyme inhibitors have been reported (Fig. 5)[9d]. Subsequently, a series of phenolic acid-amino acid conjugates was synthesized as shown in Table 3[9a–c]. Those conjugates were expected to have superoxide-scavenging activity, tyrosinase-inhibitory activity, and platelet aggregation-inhibitory activities owing to the phenolic acid moiety. However, the activities had a tendency to be weakened and the usefulness of phenolic acids regarding these three activities is decreased on the conjugates. The results indicate that we have to sort compatible combinations enhancing usefulness of each component on the conjugate.

In the research on kojic acid derivatives by Kayahara et al., combinations of components to form conjugates are compatible[10]. A typical structure of the conjugate consists of a kojic acid and an amino acid is shown in Fig. 6. The kojic acid has a whitening effectiveness owing to the tyrosinase-inhibitory activity. Table 4 shows synthetic kojic acid-amino acid(s) conjugates in their research. Most of them have more effective tyrosinase-inhibitory activity than that of the kojic acid. Especially, K-Phe-K has 376 times strong tyrosinase-inhibitory activity of kojic acid. Harmlessness of one of the kojic acid-amino acid conjugate, Ac-DL-Phe-K, has been confirmed and the research on the conjugates accomplishes a practical level.

As described, conjugates are expected not only

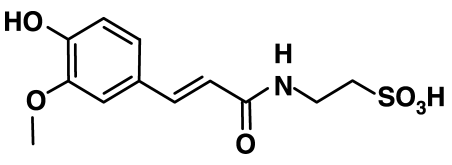


Fig. 5. Cinnamic Acid-Amino Acid Conjugate

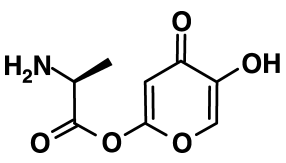


Fig. 6. Kojic Acid-Amino Acid Conjugate

Table 3. Superoxide-Scavenging Activity, Tyrosinase-Inhibitory Activity, and Platelet Aggregation-Inhibitory Activities of Phenolic Acid-Amino Acid Conjugates[9b)].

Compounds	Superoxide-scavenging activity		Tyrosinase-inhibitory activity	Platelet aggregation-inhibitory activity		
	3.0 mM	1.5 mM		Inh. r (%)		Inh. r (%)
	Inh. r (%)[a]	Inh. r (%)	Inh. r (%)	3 min	5 min	5 min.
FA-OH[b]	69.1	54.3	16.1	74.0	72.7	80.4
FA-Gly-OH	61.9	45.3	1.2	50.9	47.7	51.3
FA-Ala-OH	46.2	29.5	3.6	32.7	33.1	13.3
FA-Val-OH	34.8	29.7	0.8	23.3	22.1	13.3
FA-Leu-OH	40.5	25.2	8.0	7.5	9.3	22.8
FA-Ile-OH	41.2	26.1	9.2	-22.0	-15.1	17.7
FA-Pro-OH	30.6	27.1	0.8	8.8	9.9	12.7
FA-Phe-OH	41.5	15.2	18.4	3.8	7.0	12.7
FA-Tyr-OH	68.2	43.4	22.8	6.9	10.5	30.4
CA-OH[c]	21.7	10.5	34.5	0.0	0.0	39.2
CA-Gly-OH	24.2	5.1	16.5	22.8	19.1	19.0
CA -Ala-OH	16.0	7.0	21.7	16.5	13.5	7.6
CA -Val-OH	18.5	5.1	12.1	24.1	21.3	6.3
CA -Leu-OH	13.8	8.8	49.3	28.2	24.7	5.1
CA -Ile-OH	25.6	5.1	35.7	8.2	7.8	8.9
CA -Pro-OH	15.1	6.0	18.4	20.6	16.9	8.9
CA -Phe-OH	22.5	5.1	19.9	57.9	55.2	8.8
CA -Tyr-OH	36.3	28.8	10.7	75.4	70.7	43.9

[a] Inhibition rate [b] Ferulic acid [c] Caffeic acid

Table 4. IC_{50} Values of Amino Acid Derivatives of Kojic Acid[10b)]

Compounds	IC_{50} (mM)	Comparative value[a]	Compounds	IC_{50} (mM)	Comparative value
Z-Ala-K[b]	5.52	4.2	K-Leu-OH	14.5	1.6
Z-Thr-K	5.57	4.1	K-Leu-OBzl	13.2	2.0
Z-Val-K	2.90	7.9	K-cLeu-OMe	13.5	2.0
Z-Leu-K	4.42	5.2	K-Ile-OH	15.4	1.5
Z-Ile-K	0.86	26.7	K-Met-OH	5.1	5.2
Z-Phe-K	0.28	80.8	K-Phe-OH	8.0	2.9
Z-Tyr(OBzl)-K	1.30	17.6	K-Phe-OMe	1.6	16.6
Boc-Ala-K	13.5	1.7	K-Phe-OBzl	7.1	3.7
Boc-Val-K	22.0	1.0	K-Pro-OBzl	19.2	1.4
Boc-Leu-K	8.0	2.9	K-Tyr(OBzl)-OH	4.3	5.3
Boc-Ile-K	22.2	1.0	K-Tyr(OBzl)-OEt	3.4	7.8
H-Ala-K	53.5	0.4	K-Tyr(OBzl)-OBzl	15.2	1.8
H-Val-K	19.2	1.2	K-Asp(OBzl)-OBzl	12.6	2.1
H-Leu-K	16.1	1.4	K-Ala-K	3.0	7.6
H-Ile-K	16.9	1.4	K-Val-K	2.4	9.6
H-Tyr(OBxl)-K	1.8	12.7	K-Leu-K	2.0	11.5
K-Ala-OH	23.21	1.0	K-Ile-K	0.70	32.9
K-Val-OH	16.7	1.4	K-Phe-K	0.06	376.1
K-Val-OBzl	12.8	2.1	K-Tyr(OBzl)-K	0.49	47.0

[a] Relative activity of conjugates based on the activity of kojic acid [b] K indicates kojic acid moiety

to provide additional new functions but are also harmless. For practical use, however, many difficulties have to be clarified to meet the requirements as synthetic food additives or medicinal products.

Synthesis for Food Preparation

Although many research studies on chemical reactions in food materials typified by Maillard chemistry[11] have been carried out, these studies are intended for clarification of the reaction mechanism, not the preparation of functional foods. Hydrolysis or decomposition of a biopolymer is a major means of preparing a functional food, but synthesis of it is in disuse. As described, we can design a conjugate with better functionality than that of the components in a food material. We could also produce a useful conjugate in it to increase the value as a functional food using permissible food additives containing enzymes. This is a goal of our research. In order to reach this goal, we should carry out our research through the following three steps.

1. Design and screening of a functional conjugate in combination with components in a food material.
2. Generation of the conjugate in the food material.
3. Assurance of the safety and effect of the food containing the functional conjugate by *in vitro* and then *in vivo* assay.

The research concept is illustrated in Fig. 7. This approach for making a better functional food has good adaptability for various kinds of food materials. Our research group is now engaged in creating a functional food according to the code of this strategy and will show their attempts on this review[12].

Addition of New Functionalities to Germinated whole rice

Germinated whole rice is unmilled brown rice grains with a 0.5–1mm tall sprout that comes out after steeping in water for 22 hours at 32°C[13]. Recently, germinated whole rice has come into the public limelight as a functional food, and the market size is over 100 million yen. In germinated whole rice, the amounts of several functional compounds such as food fibers, amino acids including γ-aminobutyric acid (GABA), inositol, vitamins, minerals, tocotrienols and peptides were increased with the aid of inner enzymes. Espe-

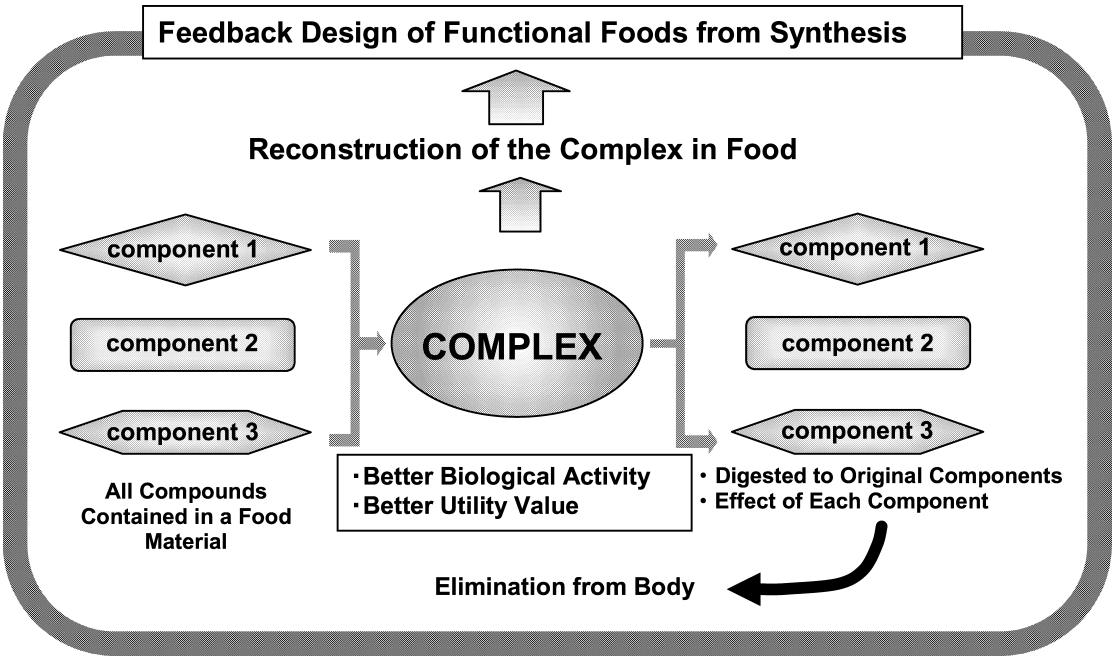


Fig. 7. Scheme of a New Functional Foods Design

cially, the amount of GABA is 10 times more than that in white rice. GABA is widely distributed in both animals and plants with a number of important biological properties. Recent reports have shown that GABA significantly lowered blood pressure in spontaneously hypertensive rats[14]. Different mechanisms to reduce blood pressure were proposed, and it is thought that the activity is induced by multiple factors. An inhibitory activity of angiotensin I converting enzyme (ACE) is one of the important factors in blood pressure decrease. Many peptidyl ACE inhibitors are known, and some of them are utilized as major components composing a functional food[15]. Recently, N-terminal sequences of rice embryo proteins have been identified by proteome analysis[16], and the several peptide fragments, which can be liberated using prolyl endopeptidase (PEP), could inhibit ACE. H-Val-Gly-Pro-OH is one of the peptides and is reported to possess ACE inhibitory activity[17]. Because GABA is a nonstandard amino acid, a GABA-containing peptide was expected to have a new function such as taste or a better ACE inhibitory activity than that of the original components, i.e., GABA, amino acids or peptides. In order to produce a new component which adds functions to germinated whole rice, GABA containing peptides were synthesized and examined regarding ACE inhibitory activity and taste. All peptides were synthesized by liquid phase procedures. The synthetic scheme of H-GABA-Val-Gly-Pro-OH is shown in Fig. 8 as an instance. Couplings were carried out using 1-ethyl-3-(-3-dimethylaminopropyl) carbodiimide hydrochloride (EDC · HCl)/1-hydroxybenzotriazole (HOBt) in DMF. Boc groups on the intermediates were cleaved by 4N HCl in dioxane, and catalytic hydrogenation (H_2/Pd) was used for the final deprotection. Other peptides were synthesized in a similar manner. The tastes of solutions of peptides/amino acid or combinations of GABA and peptide/amino acid were determined by an organoleptic test. The ACE inhibitory activity was measured according to Cushman and Cheung method[18] with some modifications. GABA has a weak ACE inhibitory activity, and several standard amino acids contained in germinated whole rice also have the same level of activity as GABA. The ACE inhibitory activity of synthetic dipeptide was vastly improved in every case (Table 5). In the combination of GABA and Phe, the ACE inhibitory activity was over 25 times the intensity of the two components. The taste of GABA was sour and the tastes of amino acids became to be bitter from sweet as the side chains lengthened. The bitter tastes of hydrophobic amino acids and the sour taste of GABA were negative factor for food. A series of synthetic GABA-dipeptides had a sweet taste in diluted solutions, and the negative tastes from the amino acids and/or GABA were weakened (Table 5). These results indicated that GABA-dipeptides could add new value as a functional food to germinated whole rice. PEP is one of the serine proteases which cleaves the C-terminal of a Pro residue in proteins or peptides and is utilized to produce food materials. Based

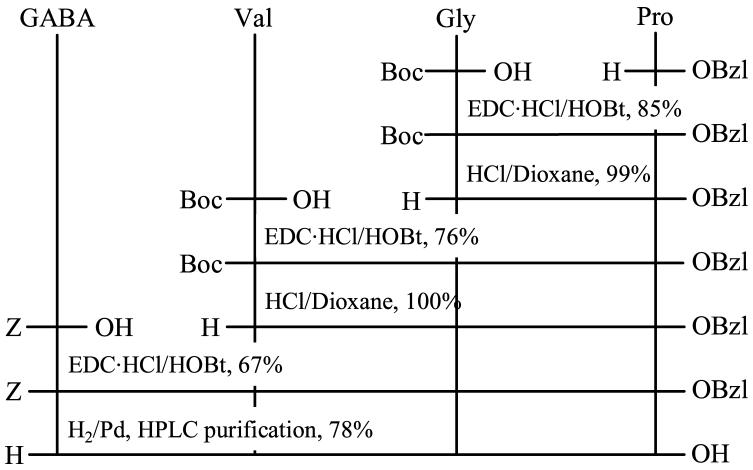


Fig. 8. Synthesis of H-GABA-Val-Gly-Pro-OH.

on the results of the GABA dipeptide, we synthesized H-GABA-Val-Gly-Pro-OH and its fragments and examined the taste and ACE inhibitory activity (Table 5). Using PEP, an ACE inhibitory peptide H-Val-Gly-Pro-OH can be liberated from the N-terminal sequence VGPVALPNLK of a rice embryo protein[16]. H-Val-Gly-Pro-OH had a relatively higher ACE inhibitory activity (26.5μM) and was almost tasteless[17]. In H-GABA-Val-Gly-Pro-OH, the inhibitory activity was the same level as H-Val-Gly-Pro-OH, and the taste was improved. H-GABA-Val-Gly-Pro-OH tasted pleasantly sweet. The results of this research indicated that the GABA peptide could improve the taste quality of food materials and that the ACE inhibitory activities of di- or tripeptides containing GABA were improved to be greater than those of the original components. Thus, it can be concluded that several GABA peptides were able to add functions to germinated whole rice.

Conclusion

Much further works are necessary for this nascent functionl food design. Among them, it is the most important to assure the safety of foods containing the conjugates. There is a possibility that a conjugate has a high-potency biologycal activitie like a drug. Functional foods should make us stay healthy, and drugs can pull us back into healthy from ill-health. Chemical drugs have saved many lives and the research on those are very important. Food science is also important as the same level as pharmaceutical sceince. In terms of necessity for everyone, food science could be more important. However, impact factors of journal generally give lower marks to food science area than pharmaceutical science area. Evaluation of effectiveness of food on us is difficult and this is one of reasons for the low valuation. We shoud challenge a new research field using leading-edge technology to face this issue. And the effort will achieve our desire to be health in whole life long.

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Table 5. Tastes and ACE Inhibitory Activities of Amino Acids, Peptides and the GABA-Peptides.

Combination of GABA and Rice Peptides	Tastes	IC_{50} (mM)
H-GABA-OH	sour	58
H-Gly-OH	sweet	49
H-Ala-OH	sweet	54
H-Val-OH	sweet/bitter	27
H-Leu-OH	bitter/sweet	39
H-Phe-OH	bitter	90
H-Tyr-OH	bitter	3.2
H-Pro-OH	flat	32
H-Val-Gly-Pro-OH	flat	0.0265[17]
H-GABA-Gly-OH	sweet	3.9
H-GABA-Ala-OH	sweet	2.0
H-GABA-Val-OH	sweet	6.8
H-GABA-Leu-OH	sweet	8.7
H-GABA-Phe-OH	sweet/bitter	2.0
H-GABA-Tyr-OH	sweet/bitter	1.6
H-GABA-Pro-OH	flat	2.8
H-GABA-Val-Gly-Pro-OH	sweet/sour	0.0213

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天然物複合体を用いた機能性食品デザイン

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要　約

将来的に、食品効果を遺伝子発現で検証しようとするニュートリジェノミックは、機能性食品研究に新しい展開をもたらし、その技術を応用した新しい効果的な機能性食品を作り出すことが可能になると考えられる。多くの機能性食品構成要素は、小分子の「複合体」としてとらえることができ、この複合体は、これまでにない新しい機能を持った安全な機能性成分となりうる。本総説では、複合体を用いた新しい機能性食品デザインと、このアイデアに沿って取り組んだ最近の研究結果を紹介する。

キーワード：機能性食品，複合体，合成，食品デザイン