

RECENT INTERPRETATION OF THE ROLE OF CERTAIN BIOCHEMICAL AGENTS*

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Up to recent times, biochemical agents in the classical sense vitamins, enzymes and hormones were classified by the criterion whether higher animal organisms, primarily man, are able to biosynthesize them (enzymes and hormones) or not (vitamins). As shown by latest experimental results, however this differentiating principle cannot be kept up, particularly in the case of vitamins. It could be shown that higher animal organisms are capable of biosynthesizing several prosthetic or inductive vitamins. Also, several recently discovered biochemical agents participate in vital processes of higher animals and in human vital processes whose vitamin character is indisputable and yet their majority is not exogenic, i.e. ingested with food, but endogenic, i.e. biosynthesized by the living organism itself [1].

Among inductive (mostly liposoluble) vitamins, vitamins A and D were first found to be biosynthesizable if a suitable precursor is present. Later — 15 years ago — the discovery of mevalonic acid gave the explanation for the biosynthesis of isoprenoids, too. This finding threw light on the origin of several recently recognized biological agents, named *bioquinones*, which — in view of their biological functions — must be considered as vitamins by up-to-date concepts.

Bioquinones are functional lipides having a quinoidal structure. They play an important role under hydrophobic conditions in electron transport, biological oxidation, oxidative phosphorylation and some specific bis-functions. A representative of this group, menaquinone or vitamin K₁ has been known for 42 years [2]. It participates in the mechanism of blood coagulation. Another representative, alpha tocopheryl quinone was found to be the conversion product of alpha tocopherol, of the compound which inhibits the oxidation of fats in fatty animal and vegetable tissues.

In general, it may be stated that most bioquinones have a terpenoid (polyprenol) side chain. This hydrophobic side chain is indispensable in their biological functions and provides the ready convertibility of bioquinones to chromane and chromene derivatives.

* Dedicated to Prof. L. Telegdy Kováts on the occasion of his 70th birthday

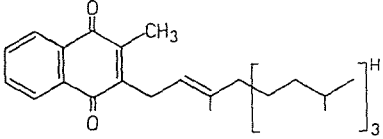
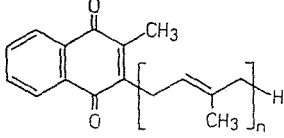
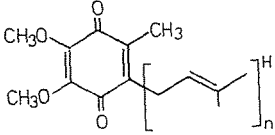
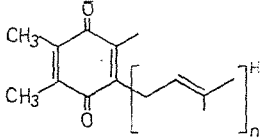
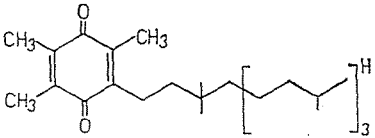
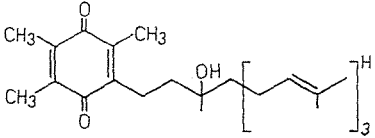
Genetical classification	IUPAC-IUB symbol	Classification according to the chemical structure	Origin	Recognized biological role
Phylloquinones and menaquinones	K	<p data-bbox="391 207 555 234">Naphtoquinones</p>  <p data-bbox="391 396 786 449">Phylloquinones: 2-methyl-3-phytyl-1,4-naphthoquinone</p>  <p data-bbox="391 611 637 700">Menaquinones: 2-methyl-3-polyprenyl-1,4-naphthoquinone $n = 1 \dots 10$</p>	Plants, animals and microorganisms	Blood coagulation, electron transport
Ubiquinones	Q	<p data-bbox="461 727 612 754">Benzoquinones</p>  <p data-bbox="391 924 798 1014">Ubiquinones: 2,3-Dimethoxy-5-polyprenyl-6-methyl-1,4-benzoquinone $n = 1 \dots 10$</p>	All aerobic organisms	Electron transport,
Plastoquinones	PQ	 <p data-bbox="391 1184 719 1256">Plastoquinones: 2,3-Dimethyl-5-polyprenyl-1,4-benzoquinone $n = 1 \dots 9$</p>	Chloroplasts	Photosynthetic electron transport, oxidative phosphorylation
Tocopheryl quinones	TQ	 <p data-bbox="391 1426 618 1453">α-Tocopheryl quinone</p>  <p data-bbox="391 1614 624 1641">α-Tocotrienyl quinone</p>	Plants and animals	Establishment of reduction-oxidation system

Fig. 1. Classification of bioquinones

The biological functions of bioquinones are manifold and not yet known in all details. It seems very probable, however, that these functions are connected with quinone-quinol conversion, with the establishment of an oxidation-reduction system.

Based on present knowledge, terpenoid quinones are classified into four main groups (Fig. 1):

— phyloquinones, menaquinones and demethyl menaquinones found in animals, plants and microorganisms, with different modes of action,

— ubiquinones occurring practically in all aerobic organisms, participating in electron transport and oxidative phosphorylation,

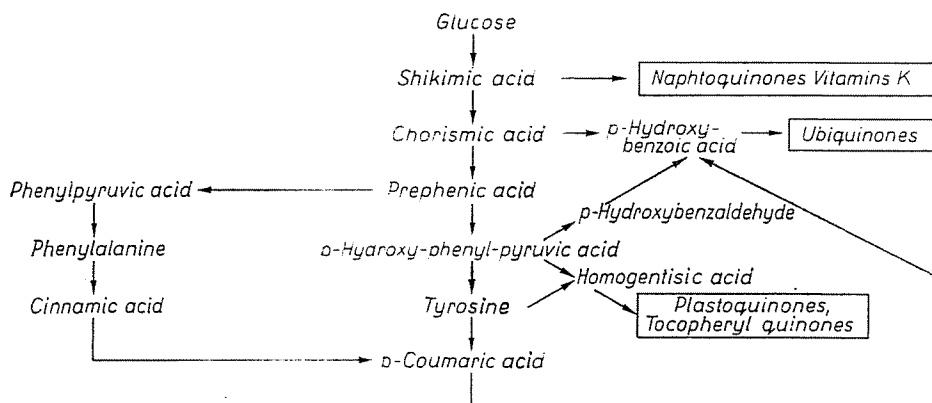


Fig. 2. Origin of the aromatic ring of bioquinones in plants

— plastoquinones which — similarly to phyloquinones — are located in chloroplasts and play a part in photosynthesis. Small amounts of plastoquinone 9 or plastoquinone A were also found in non-photosynthesizing vegetable tissues,

— tocopheryl and tocotrienyl quinones found in vegetable and certain animal tissues. Their role is not yet cleared up in all details.

With respect to their chemical structure, bioquinones consist of two groups: naphthoquinones and benzoquinones. In view of their biosynthesis in the living organism, it is an extremely interesting question how and from what compounds their aromatic rings and polyprenyl side chains are formed. Fig. 2 presents a scheme of the aromatic ring formation where shikimic acid, phenylalanine and tyrosine participate in the synthesis of the benzoquinone ring [3]. The presence of the intermediate product p-hydroxybenzoic acid was confirmed in all types of living organisms. Thus, the mechanism leading to the formation of the simple aromatic ring can be regarded as experimentally corroborated. The origin of the naphthoquinone ring, however, is still dubious, though it seems probable that its synthesis also proceeds through shikimic acid and

chorismic acid [4]. On the other hand, the synthesis of the polyprenyl side chain from mevalonic acid is quite clear (Fig. 3), as well as the most probable mechanism by which the polyprenyl side chain is coupled to the aromatic ring (Fig. 4).

Besides biosynthesis, the bioquinone demand of the living organism can also be covered by food. This is particularly valid for higher animals. For this reason, the bioquinone content of food products is also of interest.

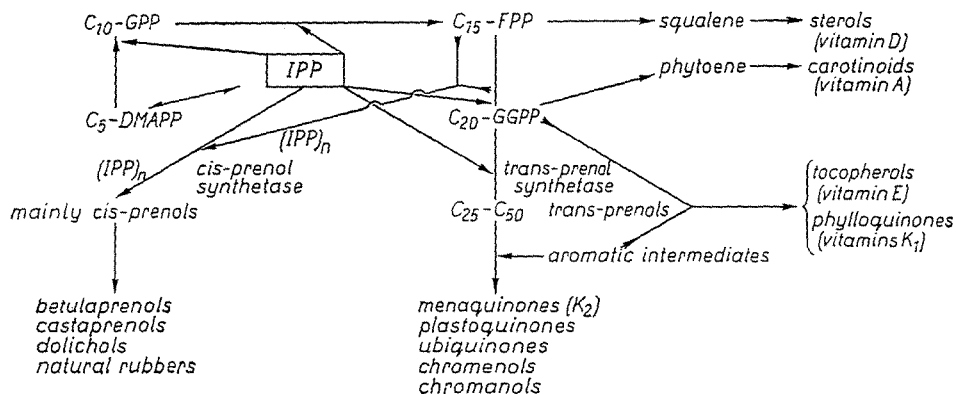


Fig. 3. Biosynthesis of polyprenyl side chains

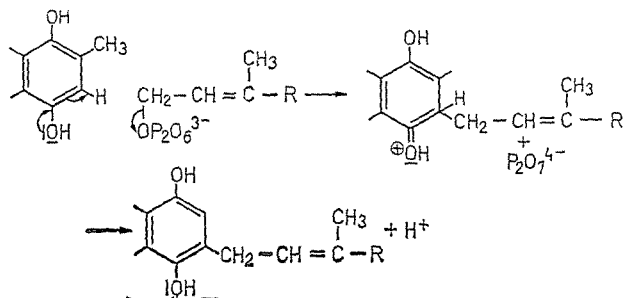


Fig. 4. Assumed coupling mechanism between the aromatic ring and the isoprenyl side chain

At the Department of Food Chemistry, we have continued systematic research work for several years together with Professor Telegdy Kováts, for obtaining answers to the following questions:

1. What is the occurrence of various kinds of bioquinones, namely phylloquinones, ubiquinones, plastoquinones, tocopheryl and tocotrienyl quinones in substances important from the view of food science? How can the individual groups and their fractions be identified? What is their quantitative distribution?

2. What changes do bioquinones undergo under various *in vitro* conditions; pH, aeration, irradiation and what are the conversion products?

3. What bioquinone losses are caused by usual food processing operations and how do these operations affect the activity of bioquinones?

These questions can be answered only if suitable methods for identification and determination are at disposal. Therefore we first developed a complex procedure for qualitative and quantitative studies of bioquinones. This was all the more important, since bioquinones are located in cell organella, in mitochondria, chloroplasts etc. and have to be isolated.

Details of the procedure were published elsewhere [5, 6]. Selected data obtained with this procedure are presented in Table 1.

These data demonstrate that the bioquinone content of the investigated Hungarian food materials is substantial. The plastoquinone content of green plants is particularly high. The ubiquinone content of various animal tissues is also considerable. The phyloquinone, menaquinone and tocopheryl quinone level of vegetable and animal substances confirms their important biochemical role.

Observations on 18 sorts of winter wheat are presented in Table 2. These data indicate a very interesting fact, namely that various kinds of bioquinones were detected in the whole grain and not alone in the germ part. This is further proof for the general occurrence of these agents. As to quantitative relations, it is particularly the ubiquinone and plastoquinone content that is considerable, followed in decreasing order by tocopheryl quinone and by the groups of phyloquinones. Animal feed wheat sorts (e.g. Etoile de Choisy, Valdichiana) are relatively rich in ubiquinones and tocopheryl quinones. Their plastoquinone content is also higher than average. In the wheat sorts for human alimentation (Bezostaya, San Pastore) the bioquinone percentages are lower. Since the data in Table 2 are the first published analytical results (at least in Central Europe), it is as yet impossible to decide whether these properties are hereditary or depend on climatic and other cultivation conditions. An exact answer to this question can be given only when results of systematic analysis for several years will be at disposal. However, already at present it seems probable that a measurable relationship exists between the wheat sort and its bioquinone content.

Research on the occurrence of bioquinones is particularly interesting in the case of living organisms where electron transport and oxidative phosphorylation proceed within the limited space of a single cell, in the case of unicellular organisms. Our data on yeasts (Table 3) show that yeasts mainly contain ubiquinones with longer side chains (Q_6 — Q_{10}) [7]. Other observations, however, displayed the systematic presence — though in very slight amounts — of ubiquinones with short side chains (Q_1 — Q_5). The low percentages indicate that the latter compounds have no significant physiological function, but are merely by-products in the biosynthesis of Q_6 — Q_{10} ubiquinones performing biological functions. It should also be mentioned that the ubiquinone content in yeasts changes with life conditions. Under aerobic conditions the Q_6 content

Table 1
Bioquinones (*K*, *Q*, *PQ*, *TQ*) of some Hungarian food stuffs

Food	<i>K</i>		<i>Q</i>		<i>PQ</i>		<i>TQ</i>	
	mg/100 g DM	ident- ified hom- ologue	mg/100 g DM	identified homologue	mg/100 g DM	ident- ified hom- ologue	mg/100 g DM	ident- ified hom- ologue
Wheat germ	0.40	<i>K</i> ₁	6.80	<i>Q</i> ₁₀	1.90	<i>PQ-A</i> , <i>PQ-C</i>	0.10	α - <i>TQ</i> γ - <i>TQ</i> traces
Maize germ	0.30	<i>K</i> ₁	7.00	<i>Q</i> ₁₀	2.30	<i>PQ-A</i> , <i>PQ-C</i>	0.20	α - <i>TQ</i>
Spinach	4.10	<i>K</i> ₁	4.90	<i>Q</i> ₁₀	10.90	<i>PQ-A</i> , <i>PQ-B</i>	0.06	α - <i>TQ</i>
Sorrel	5.43	<i>K</i> ₁	3.60	<i>Q</i> ₁₀	7.80	<i>PQ-A</i> , <i>PQ-B</i> , <i>PQ-C</i> , <i>PQ-D</i>	0.03	α - <i>TQ</i>
Lettuce	3.50	<i>K</i> ₁	1.20	<i>Q</i> ₁₀	5.90	<i>PQ-C</i> , <i>PQ-D</i>	0.01	α - <i>TQ</i>
Cabbage	2.50	<i>K</i> ₁	0.95	<i>Q</i> ₁₀	3.90	<i>PQ-C</i> , <i>PQ-D</i>	0.05	α - <i>TQ</i>
Green peas	2.00	<i>K</i> ₁	1.10	<i>Q</i> ₁₀	3.20	<i>PQ-C</i> , <i>PQ-D</i>	0.02	α - <i>TQ</i>
Brussels sprouts	3.80	<i>K</i> ₁	0.85	<i>Q</i> ₁₀	4.00	<i>PQ-C</i> , <i>PQ-D</i>	not tested	—
New potatoes	not tested	—	0.50	<i>Q</i> ₁₀	0.10	<i>PQ-A</i>	not tested	not tested
Wheat germ oil	not tested	—	1.40	<i>Q</i> ₁₀ , <i>Q</i> -9	not tested	—	2.05	α - <i>TQ</i>
Maize germ oil	not tested	—	2.20	<i>Q</i> ₁₀ , <i>Q</i> -9	not tested	—	0.98	γ - <i>TQ</i>
Sunflower oil	not tested	—	1.05	<i>Q</i> ₁₀ , <i>Q</i> -9	not tested	—	1.04	γ - <i>TQ</i> α - <i>TQ</i> traces
Chicken heart	2.80	<i>K</i> ₂	10.80	<i>Q</i> ₁₀	not tested	not tested	0.80	α - <i>TQ</i>
Chicken liver	2.00	<i>K</i> ₂	5.60	<i>Q</i> ₁₀	not tested	not tested	0.50	α - <i>TQ</i>
Turkey liver	1.50	<i>K</i> ₂	6.50	<i>Q</i> ₁₀	not tested	not tested	0.06	α - <i>TQ</i>
Beef liver	1.10	<i>K</i> ₂	3.80	<i>Q</i> ₁₀	not tested	not tested	0.70	α - <i>TQ</i>
Pork liver	1.85	<i>K</i> ₂	2.70	<i>Q</i> ₁₀	not tested	not tested	0.95	α - <i>TQ</i>
Chicken meat	0.05	<i>K</i> ₂	0.54	<i>Q</i> ₁₀	not tested	not tested	not tested	α - <i>TQ</i>
Beet meat	0.08	<i>K</i> ₂	0.95	<i>Q</i> ₁₀	not tested	not tested	not tested	—
Pork meat	0.07	<i>K</i> ₂	0.75	<i>Q</i> ₁₀	not tested	not tested	not tested	—

Table 2
Bioquinones of some Hungarian winter wheats

Material	TQ		Q		PQ		K	
	mg/100 g DM	ident- ified hom- ologue	mg/100 g DM	ident- ified hom- ologue	mg/100 g DM	identified homologue	mg/100 g DM	ident- ified hom- ologue
Miranovskaya 808	0.27	α -TQ	3.20	Q ₁₀	1.00	PQ-A, PQ-C	0.20	K ₁
Backka	0.40	α -TQ	2.90	Q ₁₀	1.10	PQ-A, PQ-C	0.28	K ₁
Dubrova	0.72	α -TQ	4.80	Q ₁₀	1.70	PQ-A, PQ-C	0.36	K ₁
San Prospero	0.20	α -TQ	3.00	Q ₁₀	1.00	PQ-A, PQ-C	0.20	K ₁
Bezostaya 1	0.20	α -TQ	2.50	Q ₁₀	1.10	PQ-A, PQ-C	0.10	K ₁
Argelato	0.47	α -TQ	4.00	Q ₁₀	2.10	PQ-A, PQ-C	0.30	K ₁
Etoile de Choisy	0.65	α -TQ	4.34	Q ₁₀	2.00	PQ-A, PQ-C	0.35	K ₁
San Pastore	0.12	α -TQ	2.20	Q ₁₀	1.50	PQ-A, PQ-C	0.25	K ₁
Lontra	0.18	α -TQ	2.70	Q ₁₀	1.00	PQ-A, PQ-C	0.20	K ₁
Libellula	0.20	α -TQ	2.50	Q ₁₀	1.10	PQ-A, PQ-C	0.18	K ₁
Brkya	0.30	α -TQ	2.95	Q ₁₀	1.70	PQ-A, PQ-C	0.09	K ₁
Rannaya	0.40	α -TQ	2.87	Q ₁₀	1.10	PQ-A, PQ-C	0.30	K ₁
Skorospelka 3/b	0.17	α -TQ	2.10	Q ₁₀	1.20	PQ-A, PQ-C	0.19	K ₁
Moisson	0.46	α -TQ	3.00	Q ₁₀	1.50	PQ-A, PQ-C	0.22	K ₁
Leonardo	0.14	α -TQ	2.00	Q ₁₀	1.10	PQ-A, PQ-C	0.09	K ₁
Pannoniya	0.57	α -TQ	4.50	Q ₁₀	2.10	PQ-A, PQ-C	0.25	K ₁
Valdichiana	0.90	α -TQ	4.50	Q ₁₀	2.00	PQ-A, PQ-C	0.20	K ₁
Lucciola	0.60	α -TQ	4.20	Q ₁₀	2.00	PQ-A, PQ-C	0.20	K ₁

of bakery yeast is five to tenfold that under anaerobic conditions. A similar increase takes place when yeast cultivated originally under anaerobic conditions is subsequently aerated.

Several of the presented data complement the data found in the world literature: up to present no reliable data were at disposal on phyloquinone, plastoquinone and tocopheryl quinone percentages in lettuce, Brussels sprouts and garden sorrel, nor on the tocopheryl quinone content in yeasts and in food of animal origin.

It is interesting to note that germ oils contain tocopheryl quinones even when quinol-quinone conversion is inhibited during processing by special measures. This finding implies that tocopheryl quinones are natural constituents of natural substances and not artefacts produced by technological operations.

The richness in bioquinones of animal and vegetable raw materials important for human alimentation underlines the necessity of intense research on the vitamin-like biological role of these constituents. This role is evidently

Table 3
Tocopheryl quinones and ubiquinones in yeasts

Test sample	Tocopheryl quinone				Total mg/100 g DM	Ubiquinone				Total mg/100 g DM
	α -TQ	β -TQ	γ -TQ	δ -TQ		Q ₆	Q ₇	Q ₈	Q ₁₀	
<i>S. cerevisiae</i> V ₃₀	+	—	—	—	0.87	+	—	—	traces	51.00
<i>S. cerevisiae</i> M ₁₉	+	—	—	—	1.10	+	—	—	traces	120.00
<i>Candida utilis</i> 14	+	—	traces	—	0.50	+	—	traces	—	48.00
<i>Torulopsis</i> 21	+	—	—	traces	1.40	+	—	—	traces	163.00
<i>S. cerevisiae</i> from Józsefváros	+	—	—	—	0.63	+	—	—	traces	28.00
<i>S. cerevisiae</i> from Óbuda (bottom yeast)	+	—	—	—	0.37	+	—	—	traces	15.12
<i>S. cerevisiae</i> from Győr	+	—	—	—	0.68	+	—	—	traces	31.20
Mixture of <i>S. cerevisiae</i> and <i>Candida tropicalis</i> C ₁₄ from Győr (bottom yeast)	+	—	+	traces	1.22	+	—	traces	—	59.41
<i>S. cerevisiae</i> from Szabadegyháza (bottom yeast)	+	—	—	—	0.34	+	—	—	traces	20.00

a complex one: in addition to the general functions of bioquinones, namely electron transport and participation in oxidative phosphorylation which are related to their structure, some bioquinones (e.g. vitamins K) possess specific functions.

Fig. 5 [8] displays the key role of ubiquinone in electron transport between flavoproteins and cytochromes.

According to recent research results, bioquinones play the part of the hitherto unknown energy transmitter in oxidative phosphorylation. Fig. 6

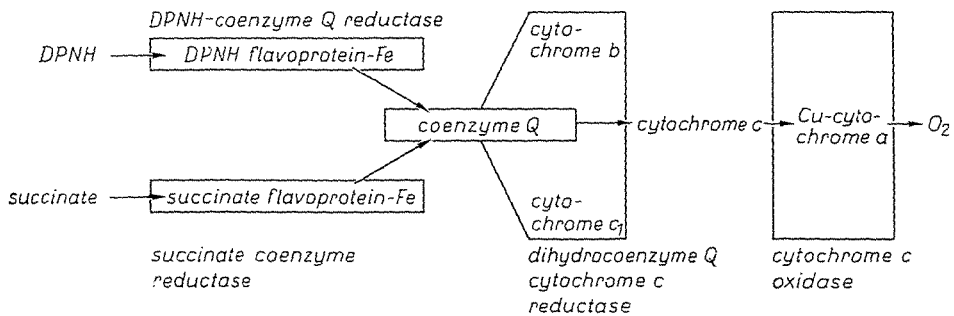


Fig. 5. Constituents of the electron transport chain complexes in mitochondrium

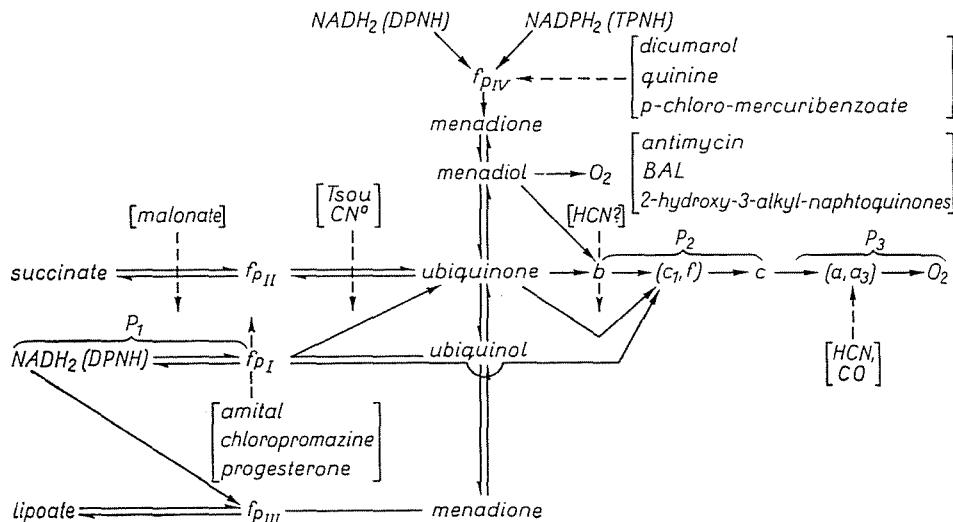


Fig. 6. Scheme of oxidative phosphorylation

presents a summary of our present knowledge on oxidative phosphorylation, showing the assumed place of natural bioquinones in the reaction mechanism [9].

This short survey on bioquinones wished to demonstrate their significance in biochemistry and in the narrower field of food chemistry and nutrition science, the necessity of further intense research and wished to motivate why the classification of certain biochemical agents, in particular of vitamins must be modified on the basis of a modern interpretation of their role and origin.

References

1. FOLKERS, K.: Internat. J. Vit. Res., **39**, 334 (1969).
2. DAM, H.: Biochem. Z., **215**, 475 (1929).
3. GLOVER, J., MORTON, R. A.: Biochemistry of Quinones. London 1965. pp. 207—255.
4. GIBSON, M. L., GIBSON, F.: Biochem. J., **90**, 248 (1964).
5. BERNDORFER-KRASZNER, É., TELEGDY KOVÁTS, L.: Élelmiszeripar, **25**, 339 (1971).
6. BERNDORFER-KRASZNER, É., TELEGDY KOVÁTS, L.: ZLUF, **148**, 8 (1972).
7. BERNDORFER-KRASZNER, É., TELEGDY KOVÁTS, L.: Szeszipar, **19**, 20 (1971).
8. FOLKERS, K., SHUNK, C. H., LINN, B. O., TRENNER, N. R., WOLF, D. E., HOFFMANN, C. H., PAGE, A. C., KONIUSZY, F. R.: CIBA Foundation Symposium on Quinones in Electron Transport. London, 1961.
9. MITCHELL, J. S., MARRIAN, D. H., MORTON, R. A.: Biochemistry of Quinones. London—New York, 1965. pp. 503—537.

Summary

In human vital processes several recently recognized biochemical agents participate whose vitamin character is indisputable and yet their majority is not ingested with food, but built up by biosynthesis in the living organism itself. Therefore it is necessary to modify the concept of biochemical agents on the basis of latest experimental results. Owing to their

quinone nature, the physiological role of bioquinones was not clear for a long time, although they participate in processes of capital importance and their majority is built up by biosynthesis in the human organism. A lesser part is ingested with food and therefore research on the bioquinone content of food raw materials and on losses caused by normal industrial processing operations is of particular interest. Several of our data complement the data found in the literature.

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