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Effects of vitamins, coenzymes and amino acids on reactions of homolytic cleavage of the *O*-glycoside bond in carbohydrates

O. I. Shadyro,* R. M. Kisel, V. V. Vysotskii and I. P. Edimecheva

Department of Chemistry of the Belarussian State University, Nezavisimosti Av., 4, 220050 Minsk, Belarus

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Abstract—It has been established that vitamins B_1, K_3 and C, coenzyme Q_0 and amino acids cysteine and histidine effectively inhibit reactions of homolytic cleavage of the *O*-glycoside bond, which are responsible for the destruction of di- and polysaccharides on γ-irradiation or the action of other reactive radical initiators. This effect was shown to originate from either oxidation or reduction of the radicals of carbohydrates undergoing destruction.

Activation of free-radical processes in biosystems results in damage to biologically important molecules, which is in many respects associated with the beginnings and development of numerous pathologic conditions.[1,2] The main role in provoking these pathophysiologic changes is attributed to oxidative processes, in particular, to lipid peroxidation.[1,2] It has been established for the first time in our studies[3–10] that reactive oxygen species, when interacting with a number of lipids, provoke destruction that occurs in the polar moiety of the latter. The key role in this process belongs to fragmentation of carbon-centred α-hydroxyl-containing radicals formed from the starting molecules, which proceeds through cleavage of two β-bonds.[3–10] In the case of cerebrosides, the reactions of such type involve rupture of the *O*-glycoside bond, which leads to formation of ceramides playing an important role in the process of apoptosis.[8,10] It should be noted that the ability of di- and polysaccharides to decompose via rupture of the *O*-glycoside bond is a characteristic feature of free-radical chemistry of carbohydrates.[11–16] The destruction of cartilaginous and conjunctive tissues, synovial fluid and eye lens, and, as a consequence, the development of arthritis, cataract and some diseases caused by the blood vessel malfunction, are thought to be, in many respects, associated with the homolytic destruction of polysaccharides,[17–21] such as hyaluronic acid and mucopolysaccharides.

Taking into account the wide prevalence of the destruction processes taking place in polysaccharides and carbohydrate-containing substances, as well as many dramatic consequences of these events, finding out substances of natural origin producing an effective influence on these processes appears to be a topical issue. For this purpose, the effects of some vitamins, amino acids and coenzyme Q_0 on the yields of products formed on radiolysis of the simplest compounds containing the *O*-glycoside bond, namely α-methyl-D-glucopyranoside (**I**) and maltose (**II**), were investigated in this study.

The starting aqueous 0.1 M carbohydrate solutions were prepared using twice-distilled water and transferred into ampoules. Before irradiation in a γ-unit (dose rates and ranges of doses absorbed are specified further in the text), the solutions in ampoules were bubbled through with argon to remove oxygen.

Analysis of destruction products, namely CH_3OH and glucose, was performed using the GC and HPLC procedures similar to those described in the following paper.[22] The compounds selected for testing were vitamins B_1, K_3 and C, coenzyme Q_0, as well as cysteine, histidine, 1,4-benzoquinone and mercaptoethanol. The respective structures, together with those of the carbohydrates, are shown in Figure 1.

Concentrations of coenzyme Q_0, Vitamins B_1 and C, cysteine, benzoquinone and mercaptoethanol varied in the range 6×10^{-6}–2×10^{-2} M, and concentrations of Vitamin K_3 and histidine were 10^{-3} M.

Keywords: Carbohydrates; Vitamin C; Vitamin B_1; Vitamin K_3; Amino acids; *O*-Glycoside bond; Free-radical fragmentation.

* Corresponding author. Tel.: +375 17 206 6146; fax: +375 17 209 5464; e-mail: shadyro@open.by

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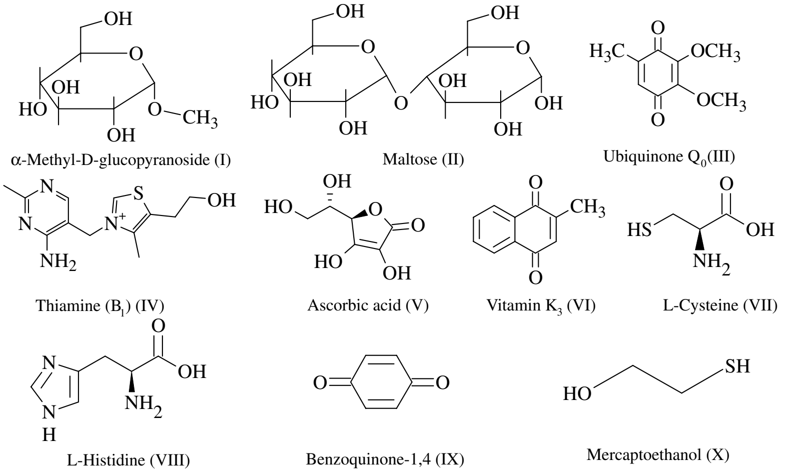

α-Methyl-D-glucopyranoside (I)

Maltose (II)

Ubiquinone Q_0(III)

Thiamine (B_1) (IV)

Ascorbic acid (V)

Vitamin K_3 (VI)

L-Cysteine (VII)

L-Histidine (VIII)

Benzoquinone-1,4 (IX)

Mercaptoethanol (X)

Figure 1. Structural formulas of the substrates and test compounds used in the study.

The effects produced by the test substances were evaluated according to changes in either accumulation of radiolysis products (Figs. 2 and 3) or radiation-chemical yields (G, mol/J) of products resulting from destruction of compounds (**I**) and (**II**) (Figs. 5 and 6).

Investigation of the effects produced by the test compounds, used at concentrations of 10^{-3} M, on yields of CH_3OH formed on radiolysis of 0.1 M solutions of compound (**I**) revealed that some of them effectively block the process of *O*-glycoside bond cleavage (cf. Fig. 2). Similar effects were observed when assessing glucose accumulation on radiolysis of deaerated aqueous 0.1 M solutions of maltose in the presence of the test substances at 10^{-3} M (Fig. 3).

Thus, it can be stated that there are substances among water-soluble vitamins, amino acids and coenzymes that are able to inhibit effectively the radiation-induced reactions involving cleavage of the *O*-glycoside bond in carbohydrates. Such effects could be explained in terms of capture by the test compounds (**III**–**X**) of $^{\bullet}$H and $^{\bullet}$OH radical species, which are formed on water radiolysis and capable of initiating destruction of substrates (**I**) and (**II**) in the absence of the inhibitors. However, this is hardly a plausible explanation because the values of rate constants for reactions of $^{\bullet}$H or $^{\bullet}$OH species with the test compounds and the carbohydrates are comparable, while concentrations of the latter are 100 times greater, which makes them the main targets.

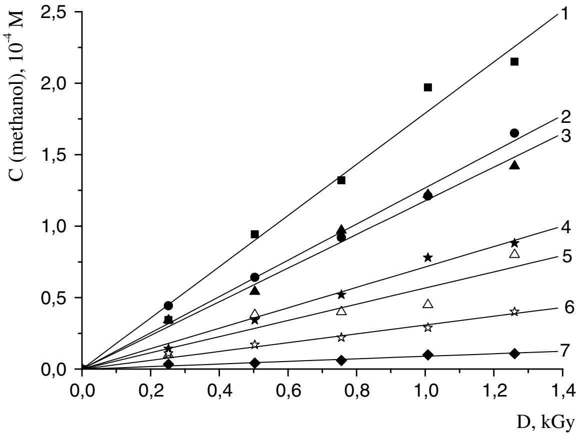

Figure 2. The effects of absorbed dose on accumulation of CH_3OH in radiolysis of 0.1 M α-methyl-D-glucopyranoside solutions in the presence of various additives: (1) in the absence of an additive, (2) vitamin K_3, (3) histidine, (4) ubiquinone Q_0, (5) vitamin C, (6) vitamin B_1, (7) cysteine. (Dose rate: 0.28 Gy/s).

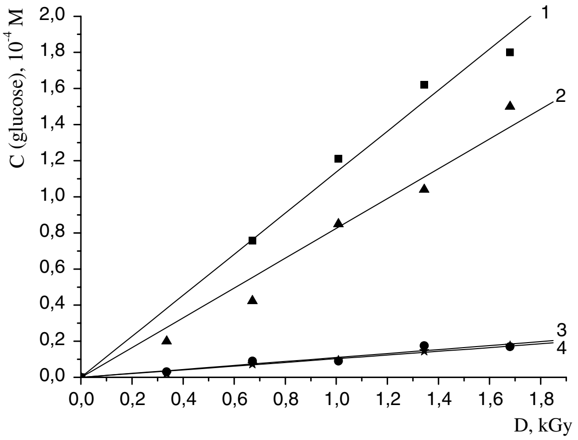

Figure 3. The effects of absorbed dose on accumulation of glucose in radiolysis of aqueous 0.1 M maltose solutions in the presence of various additives: (1) in the absence of an additive, (2) vitamin C, (3) coenzyme Q_0, (4) vitamin B_1, (dose rate: 0.28 Gy/s).

Investigation of homolytic transformations of carbohydrates initiated by γ-radiation[11–15,22] or oxidation–reduction agents[23–25] revealed that the OH-induced rupture of the *O*-glycoside bond is a key step in transformation of C-1 and C-2 radicals formed from the starting compounds. This is illustrated in Figure 4 by processes (1–3), as applied to compounds (**I**) and (**II**).

Among the processes mentioned above, only reactions (2) and (3) yield components of the starting compounds as molecular products, therefore just these reactions are