J Incl Phenom Macrocycl Chem (2012) 74:335–341
DOI 10.1007/s10847-012-0120-1

ORIGINAL ARTICLE

Organotellurium-bridged cyclodextrin dimers as artificial glutathione peroxidase models

Aiquan Jiao · Na Yang · Jinpeng Wang · Alhassane Toure · Xueming Xu · Zhengyu Jin

Received: 9 June 2011 / Accepted: 28 January 2012 / Published online: 3 March 2012

Abstract To elucidate the importance of the goodness of fit in complexes between substrates and glutathione peroxidise (GPX) mimics, we examined the decomposition of a variety of structurally distinct hydroperoxides at the expense of glutathione (GSH) catalyzed by 2,2′-ditellurobis(2-deoxy-γ-cyclodextrin) (2-Te-γ-CD), and by the corresponding derivatives of β-cyclodextrin (β-CD) and α-cyclodextrin. The good fit of the cumene group into the γ-CD binding cavity reflected the result of well-defined reaction geometry, leading to the most excellent peroxidase activity with high substrate specificity. Furthermore, the catalytic constant and the combination with the best binding also exhibited the highest regioselectivity in the substrate decomposition. Saturation kinetics were observed and the catalytic reaction agreed with a ping-pong mechanism, in analogy with natural GPX, and might exert its thiol peroxidase activity via tellurol, tellurenic acid, and tellurosulfide. The stoichiometry of the inclusion complex was determined to be of 2:1 host-to-guest. The value of stability constant K_c for $(2\text{-Te-}\gamma\text{-CD})_2$/GSH at room temperature was calculated to be $3.815 \times 10^4\ M^{-2}$, which suggested that 2-Te-γ-CD had a moderate ability to bind GSH. Importantly, the proposed mode of the $(2\text{-TeCD})_2$/GSH complex was the possible important noncovalent interactions between enzymes and substrates in influencing catalysis and binding.

Keywords Cyclodextrin dimer · Glutathione peroxidise · Artificial enzyme · Organotellurium · Molecular recognition

Introduction

Glutathione peroxidase (GPX, EC 1.11.1.9), one of the most important antioxidative selenoenzymes, protects various organisms from oxidative damage by catalyzing the reduction of harmful hydroperoxides at the expense of glutathione (GSH) [1–3]. It is related to many diseases and regarded as one of the most important antioxidant enzymes in living organisms. However, native GPX has some shortcomings, such as instability, poor availability and antigenicity, which have limited its therapeutic use [4, 5]. Additionally, it is extremely difficult to synthesize selenium-containing proteins by traditional recombinant DNA methods; therefore considerable effort has been spent to find compounds capable of imitating the properties of GPX, not only for elucidating catalytic mechanism but also for potential pharmaceutical application [6, 7].

Cyclodextrin dimers, forming inclusion complexes with binding constants comparable to that of very strong antibodies [8, 9], affect the rate of various chemical reactions with high substrate specificity, so that they have extensively been exploited as enzyme models [10–15]. Recently, a series of cyclodextrin-derived organoselenium and organotellurium compounds have been developed as GPX models with high substrate specificity [16–20]. However, β-CD, rather than α-CD or γ-CD, was used because of general availability, but again it was not clear how

Electronic supplementary material The online version of this article (doi:10.1007/s10847-012-0120-1) contains supplementary material, which is available to authorized users.

A. Jiao · N. Yang · J. Wang · A. Toure · X. Xu · Z. Jin (✉)
The State Key Laboratory of Food Science and Technology, Jiangnan University, 1800 Lihu Road, Wuxi, China
e-mail: jinlab2008@yahoo.com

A. Jiao · N. Yang · J. Wang · A. Toure · X. Xu · Z. Jin
School of Food Science and Technology, Jiangnan University, 1800 Lihu Road, Wuxi, China

important this choice was. Goodness shape/size-fitting in complexes between substrates and GPX mimics must be extremely important. The larger cavity of γ-CD-and the smaller cavity of α-CD-might change not only the catalytic rate constants within the complex but also the affinity of the catalyst to the substrate.

β-cyclodextrin dimer linked with ditelluride, as an artificial GPX model, was prepared according to the general procedure shown in scheme 1. It has been established that 2-Te-β-CD is one of the most potent catalyst found to date, compared with all other β-cyclodextrin-derived analogues. In order to extend the model system, we also prepared the corresponding derivatives of α-cyclodextrin (2-Te-α-CD) and γ-cyclodextrin dimers (2-Te-γ-CD) for investigating the relationships on substrate specificity and catalytic activity. They were synthesized by a procedure (Scheme 1) analogous to that used in the preparation of 2-Te-β-CD.

Materials and methods

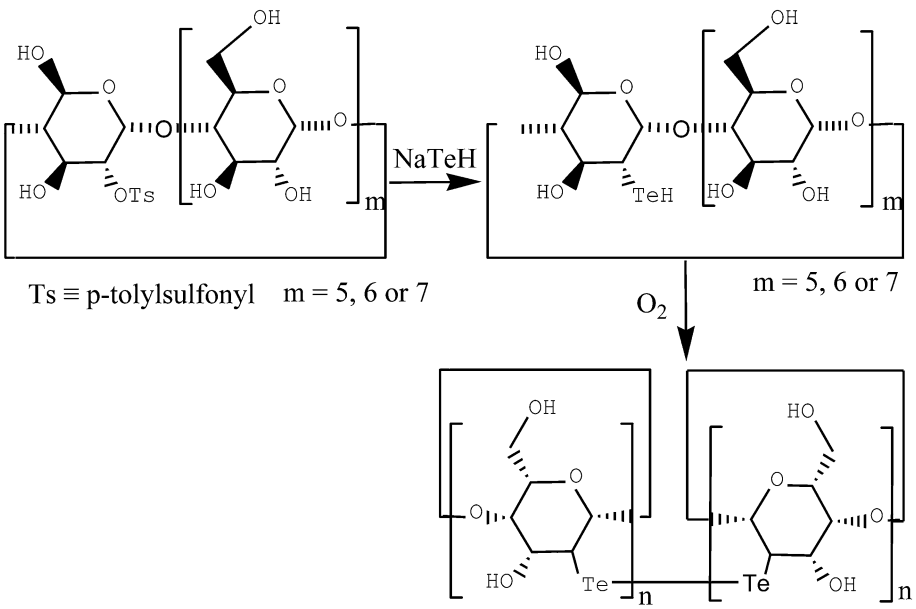
General procedure

α-, β- and γ-CD (C·P.) were obtained from the Tokyo Chemical Industry CO.LTD. *P*-toluenesulphonyl chloride (Merck), reduced glutathione (Merck) and tert-butyl hydroperoxide (Merck) were used without further purification. Tellurium powder, sodium borohydride, GSH, NADPH, CuOOH, Ebselen, and glutathione reductase (type III) were purchased from Sigma. Sephadex G-25 was purchased from Amersham Pharmacia Biotech, Uppsala, Sweden. All other chemicals were of the highest purity commercially available and were used without further purification. ^{1}H NMR and ^{13}C NMR were measured on an AVANCE III 400 MHz Digital NMR Spectrometer. IR spectra were recorded on a Nicolet NEXUS infrared spectrometer. Molecular weight was obtained from a LDI-1700 MALDI-TOF MS. The spectrometric measurements were carried out with a PERSEE TU-1900 UV–Vis-near-IR Recording Spectrophotometer interfaced with a personal computer. Data were acquired and analyzed by using UV spectroscopy software. The temperature for UV time course studies was controlled within (±) 0.5 °C by use of a LAUDA compact low-temperature thermostat RC6 CP. The concentrations of the hydroperoxide stock solutions were determined by titration with potassium permanganate. Phosphate buffer (PBS) was used in all experiments.

Synthesis of GPX mimics (1), (2) and (3)

The synthesis method of GPX mimics is shown in Scheme 1. In the first step, the regiospecific monotosylation of the 2-position hydroxy group of each cyclodextrin was carried out according to the method described by Fujita et al. [21, 22]. NaTeH was prepared according to the method described by Klayman et al. (1973) [23]. Subsequently, 2-O-(4-Methylbenzenesulfonyl)-CD (100 mg) was dissolved in PBS (10 mL, 50 mM, pH 7.0), and then

Scheme 1 Synthesis of GPX mimics (1), (2) and (3)



(1): 2,2'-ditellurobis(2-deoxy-α-cyclodextrin) (2-Te-α-CD) (n=6)
(2): 2,2'-ditellurobis(2-deoxy-β-cyclodextrin) (2-Te-β-CD) (n=7)
(3): 2,2'-ditellurobis(2-deoxy-γ-cyclodextrin) (2-Te-γ-CD) (n=8)

NaTeH (100 μL, 1 M) was added under the protection of pure nitrogen. Following a reaction period of 48 h at 60 °C, the reaction mixture was oxidized in air sufficiently. In the final step, the reaction mixture was purified by centrifugation and Sephadex G-25 column chromatography ($\lambda = 254$ nm) with deionized water as the eluent. The product solution was freeze-dried and the lyophilized power provided the products (1–3) with a yield of 65, 62, and 57%, respectively.

Characterization of (1) (2-Te-α-CD)

^{1}H NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 5.47$–4.98 (m, 12H, H-1), 3.95–3.60 (m, 48H, H-3, H-5, H-6), 3.48–3.22 ppm (m, 24H, H-2, H-4); ^{13}C NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 100.4$–98.5(C1), 80.2–78.3(C4), 71.2–68.6(C2, C3, C5), 59.7(C6), 51.0 ppm ($C2^A$); IR (cm^{-1}, KBr): 3380, 1397 (−OH), 2927 (CH, CH_2), 1633, 1153, 1078, 1029 (−O−); MALDI-MS: calcd. 2166.8, found 2167.3; elemental analysis calcd (%) for $C_{72}H_{118}O_{58}Te_2{\cdot}6H_2O$: C 38.01, H 5.76; Found: C 37.95, H 5.69.

Characterization of (2) (2-Te-β-CD)

^{1}H NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 4.99$ (m, 14H, H-1), 4.0–3.65 (m, 56H, H-3, H-5, H-6), 3.65–3.28 ppm (m, 28H, H-2, H-4); ^{13}C NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 100.8$, 98.5(C1), 80.1(C4), 75.9–68.3(C2, C3, C5), 59.5(C6), 50.8 ppm ($C2^A$); IR (cm^{-1}, KBr): 3367, 1404 (−OH), 2928 (CH, CH_2), 1630, 1154, 1083, 1027 (−O−); MALDI-MS: calcd.2599.2, found 2599.7; elemental analysis calcd (%) for $C_{84}H_{138}O_{68}Te_2{\cdot}6H_2O$: C 38.32, H 5.58; Found: C 37.85, H 5.64.

Characterization of (3) (2-Te-γ-CD)

^{1}H NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 5.44$–4.90 (m, 16H, H-1), 3.77–3.42 (m, 64H, H-3, H-5, H-6), 3.39–3.07 ppm (m, 32H, H-2, H-4); ^{13}C NMR (400 MHz, D_2O, 25 °C, TMS): $\delta = 99.8$–98.1(C1), 79.5–77.8(C4), 70.7–67.2(C2, C3, C5), 59.5(C6), 50.5 ppm ($C2^A$); IR (cm^{-1}, KBr): 3370, 1400 (−OH), 2928 (CH, CH_2), 1630, 1155, 1080, 1030 (−O−); MALDI-MS: calcd. 2815.4 found 2815.9; elemental analysis calcd (%) for $C_{96}H_{158}O_{78}Te_2{\cdot}6H_2O$: C 39.44, H 5.86; Found: C 39.45, H 5.84.

Procedures of estimation of GPX-like activity

The GPX-like activity of the mimics catalyzed reduction of hydroperoxide by GSH was assessed by using coupled reductase assay with minor modification [24]. The sample and control cuvettes both contained PBS (50 mM, pH 7.0), sodium azide (1 mM), EDTA (1 mM), GSH (0.1 mM), ROOH (0.25 mM), NADPH (0.25 mM), GSH reductase (1 U), and a moderate amount of test compound at 37 °C. This reaction was started by the subsequent addition of ROOH and the absorbance at 340 nm was recorded for a few minutes to determine the rate of NADPH consumption. One unit of enzyme activity was defined as the amount of enzyme mimic that used 1 μmol NADPH per min.

Procedures of assay of kinetics of mimics

The enzymatic mimic-catalyzed reduction and nonenzymatic reduction of hydroperoxides by GSH were monitored by observation of the decrease in NADPH absorbance at 340 nm at 37 °C. In order to investigate the relationship between the reaction rate and the substrate concentration, the initial velocities were determined by varying one substrate concentration while the other was kept constant. All kinetic experiments were performed at 37 °C in 1 mL of reaction solution containing PBS (50 mM, pH 7.0), and appropriate concentrations of GSH, hydroperoxides, and 2-Te-CD. All reaction conditions and the procedure were similar to that of the estimation of GPX-like activity. The reaction was initiated by the addition of the ROOH. The enzymatic rates were corrected for the background (nonenzymatic) reaction between hydroperoxides and GSH.

^{1}H NMR study on the inclusion complex of GSH with 2-Te-γ-CD

GSH was dissolved in D_2O (concentration of 10 mM was used). GSH solution was separated into two portions. A portion was used as a guest NMR sample, and the remainder was used to dissolve and to dilute the sample of the host, so that the concentration of GSH remained constant throughout the titration. Successive aliquots of the host solution were added to GSH sample, and ^{1}H NMR spectra were recorded after each addition. Samples for ^{1}H NMR measurements were prepared directly in an NMR tube by adding appropriate amounts of the host and a guest with a microsyringe.

Results and discussion

GPX activity of GPX mimics

The GPX-like activities of three mimics are given in Table 1 by using the classical coupled reductase assay [24], in which the oxidation of NADPH was spectrophotometrically monitored at 340 nm by coupling to the reduction of the oxidized glutathione (GSSG) catalyzed by glutathione reductase. For the peroxidase activity, the enzymatic

catalytic activities were corrected for the background (nonenzymic) reaction between hydroperoxide and GSH. As shown by the data, cyclodextrin-derived GPX mimics with hydrophobic cavity had much higher peroxidase activity than Ebselen, which carried no binding group for substrates. Obviously, substrate binding played a vital role in GPX catalysis. Hydroperoxides decomposing capacity of 2-Te-γ-CD was determined to be 80.5, 109.8, 149.6 U/μmol, respectively, with hydrogen peroxide (H_2O_2), tert-butyl hydroperoxide (t-BuOOH) and cumene hydroperoxide (CuOOH), which was almost 81.3, 332.7, 118-fold than that of Ebselen. Analyzing the different activities among cyclodextrin-derived organotellurium compounds, there was a trend that catalytic efficiency increased with increasing size of the cavity of cyclodextrin. Thus, the following order of catalytic efficiency was found with H_2O_2, t-BuOOH and CuOOH as substrates: (3) > (2) > (1). Furthermore, the notable result from the coupled reductase assay was the specificity for reduction of aryl CuOOH. Unlike mimics (1), GPX mimics (2) and (3) were substrate specific and the preferred substrate was CuOOH. It is expected that the bulky aromatic group of CuOOH binds fairly strongly into β- or γ-CD, so as to bring the HOO group into close proximity to tellurium at the secondary face of the cyclodextrin, but apparently with geometry that did not permit the interaction with α-CD. It therefore seemed that the binding of the substrate ROOH was the key step in the catalysis process.

Kinetics of GPX mimics catalyzed reduction of peroxides by GSH

To probe the mechanism by which the mimics promote the peroxidase reaction, detailed kinetic studies were undertaken. Mugesh and co-workers had confirmed that catalyst-substrate complex did exist during the catalytic cycle through a detailed kinetic study [25]. Herein, we did similar kinetic experiments to characterize the catalyst-substrate complex. By varying the concentration of GSH while the concentration of catalyst was maintained constant, we were able to obtain saturation plots (Fig. 1) and such saturation behaviour may be generally regarded as evidence for complex formation between mimics and substrates [26]. At the same time, when the concentration of 2-TeCD was increased, the rates became very high for higher concentrations of GSH. From this observation, it was clearly shown that the intermediate (CDTeSG) did exist during the catalytic cycle. Double reciprocal plots (see supporting information) of the initial velocity versus the concentration of substrates yielded the characteristic parallel lines of a Ping-Pong mechanism with at least one covalent intermediate [27], in analogy with natural GPX. The apparent kinetic parameters obtained at several GSH and hydroperoxides concentrations were summarized in Table 2. These values were deduced from the relevant steady-state equation (eq. 1) of a Ping-Pong kinetic mechanism.

$$\frac{v_0}{[E]_0} = \frac{k_{\max}[GSH][ROOH]}{K_{ROOH}[GSH] + K_{GSH}[ROOH] + [GSH][ROOH]} \quad (1)$$

In this model, v_0 is the initial reaction rate, $[E]_0$ is the initial enzyme mimic concentration, k_{max} is a pseudo-first-order rate constant and K_{ROOH} and K_{GSH} are the Michaelis–

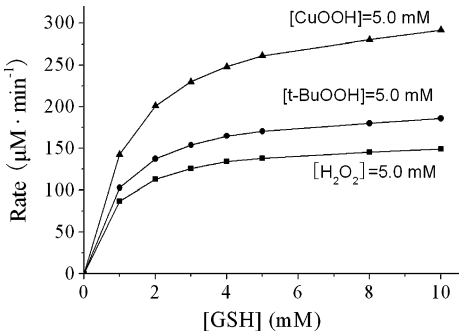


Fig. 1 A representative plot of initial rates (v_0) at different concentrations of the substrate and at 2 μM mM of catalyst (3). The initial ROOH concentration was fixed at 5 mM

Table 1 The activity for the reduction of hydroperoxide by GSH in the presence of various catalysts at pH 7.0 and 37 °C[a].

Mimics	Activity of different hydroperoxides (U/μmol)		
	H_2O_2	t-BuOOH	CuOOH
Ebselen	0.99 ± 0.01	0.33 ± 0.01	1.26 ± 0.01
(1)	34.4 ± 0.17	23.8 ± 0.10	–
(2)	46.7 ± 0.20	32.3 ± 0.15	87.3 ± 0.26
(3)	80.5 ± 0.36	109.8 ± 0.38	149.6 ± 0.43

[a] One unit of enzyme activity is defined as the amount of mimic that utilizes 1 μmol of NADPH per minute. All values are means of at least five times with standard deviation

Table 2 Kinetic parameters for the mimics-catalyzed reduction of hydroperoxides by GSH. All data are presented as means ± SD

Mimics	Constant	ROOH (× 10^4 M^{-1} min^{-1})		
		H_2O_2	t-BuOOH	CuOOH
(**1**)	k_{max}/K_{ROOH}	4.47 ± 0.02	2.85 ± 0.01	–
	k_{max}/K_{GSH}	4.81 ± 0.02	3.17 ± 0.01	–
(**2**)	k_{max}/K_{ROOH}	7.99 ± 0.04	5.24 ± 0.02	27.1 ± 0.12
	k_{max}/K_{GSH}	6.28 ± 0.03	6.26 ± 0.03	6.86 ± 0.03
(**3**)	k_{max}/K_{ROOH}	11.8 ± 0.05	15.5 ± 0.05	36.3 ± 0.15
	k_{max}/K_{GSH}	9.33 ± 0.04	10.4 ± 0.07	12.6 ± 0.05

Menten constants for the ROOH and GSH, respectively.The k_{max}/K_{ROOH} values for (**2**) and (**3**), as shown in Table 2, varied in the order $k_{max}/K_{CuOOH} > k_{max}/K_{t\text{-}BuOOH} > k_{max}/K_{H2O2}$, whereas (**1**) lacked of a capacity to decompose CuOOH by GSH. This clearly revealed that the GPX mimic based on cyclodextrin had substrate specificity for substrate hydroperoxide in the enzymatic reaction. The k_{max}/K_{GSH} value for (**3**) was 1.26×10^5 M^{-1} min^{-1}, which did allow an approximate comparison with that of the native GPX (1.93×10^6) as determined previously [28].

^{1}H NMR study on the inclusion complex of GSH with 2-Te-γ-CD

To obtain the mechanism of 2-Te-γ-CD promoting the peroxidase reaction with the highest activity, the interaction between 2-Te-γ-CD and GSH was investigated in D_2O at room temperature by ^{1}H nuclear magnetic resonance (^{1}H NMR) technique. ^{1}H NMR spectroscopy is one of the most important methods for investigating the stability and stoichiometry of complexes. The NMR spectra of most CD complexes represent concentration-weighted averages since exchange between the complexed and free guest molecule was fast in the NMR time scale. Therefore, to determine association constants with CDs, nonlinear fitting of chemical shift changes as a function of concentration (the so-called NMR titration) is usually performed [29]. Fig. 2 presented ^{1}H NMR spectra of (a) GSH, (b) 2-Te-γ-CD and (c) the mixture of GSH and 2-Te-γ-CD at the room temperature. The ^{1}H NMR spectra of the GSH showed significantly upfield shifts upon addition of 2-Te-γ-CD, while the signals of the 2-Te-γ-CD recorded in the presence of GSH also showed some differences with respect to those of 2-Te-γ-CD alone. In particular, not only internal protons (H3 and H5) of 2-Te-γ-CD underwent upfield shifts in the presence of equimolar amounts of GSH, but also did the outer protons (H2 and H4). This may be attributed to interaction dominated by hydrogen bonding, which is different from that of most complexes studied previously [30, 31]. It can be taken as an indication of the occurrence of a 'host–guest' interaction.

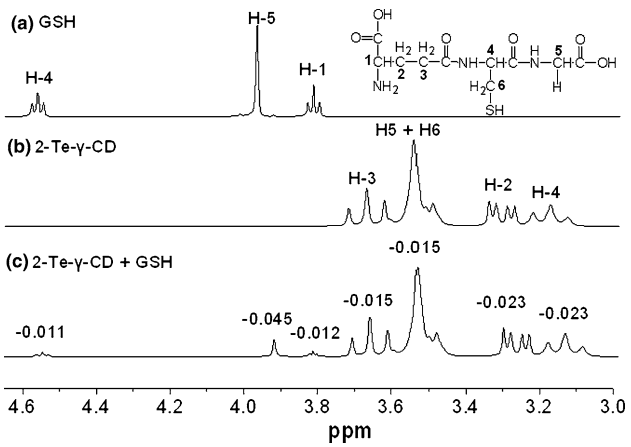


Fig. 2 ^{1}H NMR spectra at room temperature in D_2O of *a* 10 mM GSH, *b* 10 mM 2-Te-γ-CD and *c* the mixture of 10 mM 2-Te-γ-CD and 10 mM GSH, respectively

The experimental NMR spectra represented the concentration-weighted average of the spectra of GSH/2-Te-γ-CD complex in water. Therefore, the association constant and stoichiometry between GSH and 2-Te-γ-CD could be calculated by the concentration dependence of the chemical shifts ($\Delta\delta$) of GSH. Because the differences of the resonance frequency of the H-5 proton was well resolved and considerably intense, the chemical shifts of the H5 proton in GSH were measured from the NMR spectra (see supporting information). The stoichiometry of the inclusion complex was determined to be of 2:1 host-to-guest by the molar method. According to the procedure of Ishizu [32], the value of the stability constant K_c for (2-Te-γ-CD)$_2$/GSH at room temperature was calculated to be 3.815×10^4 M^{-2}, which suggested that 2-Te-γ-CD had a moderate ability to bind GSH. The detail of deduced process is described as follows.

The stability constant of the complex K_c (M^{-1}) is represented in eq. 2, where [G], [H], and [H_2G] are the mole concentration of GSH, 2-Te-γ-CD, and the (2-Te-γ-CD)$_2$/GSH complex (mM), respectively, and $[G]_0$ and $[H]_0$ were the initial concentration (mM) of guest and host respectively. In eq. 4, δ_{GSH}, δ_{H2G} and δ_{obs} represented the chemical shift (ppm) of H-5 of GSH, the inclusion complex of (2-Te-γ-CD)$_2$/GSH and the mixture of 2-Te-γ-CD with GSH in ^{1}H NMR spectra, respectively [33].

$$K_c = \frac{[H_2G]}{[G][H]^2} = \frac{[H_2G]}{([G]_0 - [H_2G])([[H]_0 - 2[H_2G])^2} \quad (2)$$

which on rearrangement transformed to

$$\frac{1}{K_c} = \left(\frac{[G]_0}{[H_2G]} - 1\right)([H]_0 - 2[H_2G]\Big)^2$$

$$\frac{1}{[G]_0^2 K_c} = \left(\frac{[H]_0}{[G]_0} - \frac{2[H_2G]}{[G]_0}\right)^2 \left(\frac{[G]_0}{[H_2G]} - 1\right) \quad (3)$$

θ was expressed as

$$\theta = \frac{[G]_0 - [G]}{[G]_0} = \frac{[H_2G]}{[G]_0} \quad (4)$$

The observed chemical shift (ppm) of H5 of GSH would be given by

$$\delta_{obs} = \delta_G(1-\theta) + \delta_{H_2G}\theta$$

$$\delta_{obs} = \delta_G(1-\theta) + \delta_{H_2G}\theta = \frac{\delta_G - \delta_{obs}}{\delta_G - \delta_{H_2G}} = \frac{\Delta\delta_{obs}}{\Delta\delta_{H_2G}}$$

M was expressed as

$$M = \frac{[H]_0}{[G]_0} \tag{5}$$

Combining eqs. 3–5 gave

$$\frac{1}{[G]_0^2 K_c} = \left(\frac{1}{\theta} - 1\right)(M - 2\theta)^2 \tag{6}$$

Which on rearrangement transformed to

$$M = 2\theta \pm \frac{1}{[G]_0}\sqrt{\frac{\theta}{(1-\theta)K_c}}$$

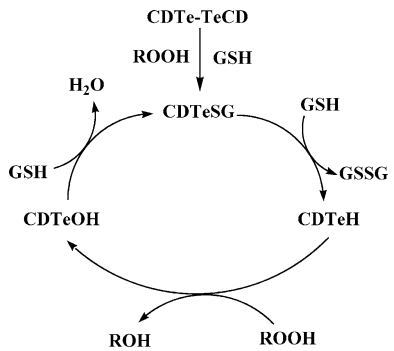
Combining eqs. 6, 4, and 5 and transforming gave

$$[H]_0 = \frac{2\Delta\delta_{obs}}{\Delta\delta_{H_2}G}[G]_0 \pm \sqrt{\frac{\Delta\delta_{obs}}{(\Delta\delta_{H_2}G - \Delta\delta_{obs})K_c}} \tag{7}$$

The K_c value at room temperature was estimated from the change in $\Delta\delta_{obs} = (\delta_G - \delta_{H2G})$ versus increasing $[H]_0$ at constant $[G]_0$ using eq. 7. Although the current NMR data were not able to describe the detailed conformation of the (2-Te-γ-CD)$_2$/GSH complex, it could be sure that the interaction between 2-Te-γ-CD and GSH did exist in the complexation.

Mechanism for the catalytic activity

Based on experimental data above, we proposed a possible mechanism for the catalytic activity of compounds 2-Te-CD as shown in Scheme 2. According to this mechanism, the role that tellurium played in biochemistry is similar to the role that selenium played in the thiol peroxidase reaction of native GPX. The catalytic cycle of 2-Te-CD involved some major steps. In the presence of hydroperoxide, ditellurium-bridged cyclodextrin dimer reacted with GSH to give tellurosulfide (CDTeSG). A second GSH generated the active tellunol (CDTeH) by attacking the CDTeSG to form the oxidized glutathione (GSSG). The tellunol was then oxidized to a tellurenic acid (CDTeOH), which reacted with GSH to reform the tellurosulfide. The tellurium underwent a redox cycle involving a key intermediate CDTeSG. However, a detailed characterization of the intermediates was needed to investigate the mechanistic role of various organotellurium intermediates in the catalytic cycle. As indicated above, 2-TeCD exerted their peroxidase activity via tellurosulfide, tellurol, and tellurenic acid, while the differences in the relative activities of the ditellurides were due to the varying degree of goodness of fit in complexes between substrates and mimics.



Scheme 2 Proposed Catalytic Mechanism of 2-Te-CD

Acknowledgments We are grateful to Dr. Kim for providing language help, Dr. Z.F. Li and C.Y. Ma for their technical assistance, and Miss W.H. Cui and G.Q. Wang for secretarial assistance. This study was supported by National Natural Science Foundation of China (No. 20976070), Project of Education Ministry (No. 109080), Nature Science Foundation of Jiangsu Province (Nos. BK2008003 and BK2009069).

References

1. Rotruck, J.T., Pope, A.L., Ganther, H.E., Swanson, A.B., Hafeman, D.G., Hoekstra, W.G.: Science **179**, 4073 (1973)
2. Mugesh, G., du Mont, W–.W., Sies, H.: Chem Rev **101**, 2125 (2001)
3. Mugesh, G., du Mont, W.-W.: Chem Eur J **7**, 1365 (2001)
4. Sies, H.: Free Radic Biol Med **14**, 313 (1993)
5. Liu, J-q, Luo, G-m, Ren, X-j, Mu, Y., Bai, Y., Shen, J-c: Biochim Biophys Acta **1481**, 222 (2000)
6. Tan, K.-L., Chelvanayagam, G., Parker, M.W., Board, P.G.: Biochem J **319**, 315 (1996)
7. Bhabak, K.P., Mugesh, G.: Chem Eur J **16**, 1175 (2010)
8. Breslow, R., Chung, S.: J Am Chem Soc **112**, 9659 (1990)
9. Venema, F., Nelissen, H.F.M., Berthault, P., Birlirakis, N., Rowan, A.E., Feiters, M.C., Nolte, R.J.M.: Chem Eur J **4**, 2237 (1998)
10. D'Souza, V.T.: Supramol Chem **15**, 221 (2003)
11. Marinescu, L., Molbach, M., Rousseau, C., Bols, M.: J Am Chem Soc **127**, 17578 (2005)
12. Bjerre, J., Fenger, TH., Marinescu, LG., Bols, M.: Eur J Org Chem:704 (2007)
13. Breslow, R., Dong, S.D.: Chem Rev **98**, 1997 (1998)
14. Lopez, O.L., Marinescu, L., Bols, M.: Tetrahedron **63**, 8872 (2007)
15. Thomas, H.F., Bjerre, J., Bols, M.: ChemBioChem **10**, 2494 (2009)
16. Luo, G-m, Ren, X-j, Liu, J-q, Mu, Y., Shen, J-c: Curr Med Chem **10**, 1151 (2003)
17. Ren, X., Xue, Y., Liu, J., Zhang, K., Zheng, J., Luo, G., Guo, C., Mu, Y., Shen, J.: ChemBioChem **3**, 356 (2002)
18. McNaughton, M., Engman, L., Birmingham, A., Powis, G., Cotgreave, I.A.: J Med Chem **47**, 233 (2004)
19. Dong, Z.-Y., Huang, X., Mao, S.-Z., Liang, K., Liu, J.-Q., Luo, G.-M., Shen, J.-C.: Chem Eur J **12**, 3575 (2006)
20. Jamier, V., Ba, L.A., Jacob, C.: Chem Eur J **16**, 10920 (2010)

21. Onozuka, S., Kojima, M., Hattori, K., Toda, F.: Bull Chem Soc Jpn **53**, 3221 (1980)
22. Fujita, K., Tahara, T., Koga, T., Imoto, T.: Bull Chem Soc Jpn **62**, 3150 (1989)
23. Klayman, D.L., Griffin, T.S.: J Am Chem Soc **95**, 197 (1973)
24. Wilson, S.R., Zucker, P.A., Huang, R.R.C., Spector, A.: J Am Chem Soc **111**, 5936 (1989)
25. Mugesh, G., Panda, A., Singh, H.B., Punekar, N.S., Butcher, R.J.: J Am Chem Soc **123**, 839 (2001)
26. Yoon, CJ., Ikeda, H., Kojin, R., Ikeda, T., Toda, F.: J Chem Soc Chem Commun:1080 (1986)
27. Dalziel, K.: Biochem J **114**, 547 (1969)
28. Flohe, L., Loschen, G., Guenzler, W.A., Eichele, E.: Hoppe-Seyler's Z. Physiol Chem **353**, 987 (1972)
29. Paola, F., Marco, L., Elisabetta, M., Franco, P.G.: J Am Chem Soc **126**, 4343 (2004)
30. Schneider, H.-J., Hacket, F., Ruediger, V., Ikeda, H.: Chem Rev **98**, 1755 (1998)
31. Rekharsky, M.V., Inoue, Y.: Chem Rev **98**, 1875 (1998)
32. Ishizu, T., Kintsu, K., Yamamoto, H.: J Phys Chem B **103**, 8992 (1999)
33. Bergeron, R.J., Channing, M.A., Gibeily, G.J., Pillor, D.M.: J Am Chem Soc **99**, 5146 (1977)