New β-Hydroxyaspartate Derivatives Are Competitive Blockers for the Bovine Glutamate/Aspartate Transporter*

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Four subtypes of excitatory amino acid transporters (EAAT1–4) have been identified in the mammalian brain. A number of pharmacological agents have been developed to study their intrinsic properties and function. Up to now, blockers were available only for EAAT2, whereas all the inhibitors of glutamate uptake active on the other subtypes were proved to be substrates of the transporters. We synthesized five new derivatives of DL-threo-β-hydroxyaspartic acid, a well known general substrate of EAATs, and investigated their potential blocking activity on the cloned bovine EAAT1 expressed in the Xenopus oocyte system, by using radiotracer and voltage-clamp techniques. Two of our derivatives proved to be substrates for bovine EAAT1, with reduced electrogenericity compared with their parent compound, and an affinity of 40 and 64 μM. The last three derivatives displayed a blocking activity on bovine EAAT1. The affinity of threo-β-benzoyloxyaspartate and threo-β-(1-naphthoyl)oxyaspartate was determined by Schid analysis as 17.2 and 52.1 μM, respectively. These blockers should help in the better understanding of the key intrinsic properties of EAAT1. Moreover, they appear as good candidates for a general blocking activity on EAATs.

Reuptake of the excitatory neurotransmitter L-glutamate in the mammalian central nervous system is mediated by specific high affinity transporters that couple the electrochemical gradient of co-transported sodium and counter-transported potassium ions to that of glutamate (1, 2). A co-transport of proton also occurs during glutamate transport (3). Recently, several members of a new gene family encoding excitatory amino acids transporters (EAAT)1 have been cloned from rodents, EAAT1 (GLAST) (4–6), EAAT2 (GLT-1) (7), and EAAT3 (EAAC1) (8). Homologous transporters have been identified in bovine brain, EAAT1 (BGLAST) (9) and human brain (EAAT1–3) (10–13), and a fourth subtype was cloned from human brain (EAAT4) (14). Whereas EAAT3 has been shown to be of neuronal origin (15, 16), EAAT1 and 2 are astroglial transporters (15–17). These transporters are differentially expressed in various brain regions (12, 15, 16). The importance of EAATs in limiting the extracellular concentration of glutamate, and therefore its excitotoxicity, was suggested by the substantial loss of the glial transporter, EAAT2, in the chronic degenerative disorder, amyotrophic lateral sclerosis (15). Furthermore, recent knock-out experiments of the genes encoding EAATs have demonstrated the major role of astroglial transport in maintaining low extracellular glutamate and for preventing chronic glutamate neurotoxicity (18).

A number of glutamate analogs have been shown to inhibit the transport of radiolabeled glutamate (19–22). As substrate uptake by EAATs is electrogenic, transport can be measured in real time using voltage-clamp (23–26). This makes possible the distinguishing of inhibitors acting as competitive substrates and those acting as blockers (12). Up to now, only kainate and dihydrokainate have been shown to block EAATs, and they displayed high affinity only for EAAT2 (12). Indeed kainate proved useful for obtaining kinetic information on this transporter (27). Such kinetic data are of primary importance for the evaluation of how transporters modulate glutamatergic transmission. Kainate was also used to reveal a substrate-independent leak conductance in the human EAAT1 (28). Nevertheless, the insensitivity of EAAT1 toward kainate had first to be overcome by the construction of a chimerical transporter comprising part of the substrate binding site of EAAT2. The development of selective blockers for each of the EAATs’ subtype and/or of general blockers is therefore greatly needed.

We designed blockers of EAATs by modifying the structure of a well known general substrate. The starting compound, DL-threo-β-benzoyloxyaspartate (THA) has been demonstrated to be a well known general substrate. The starting compound, DL-threo-β-hydroxyaspartate (THA) has been demonstrated to be a good candidate for a general blocking activity on bovine EAAT1, the most potent of them displaying an affinity of 17.2 μM. These molecules are the first blockers ever described for EAAT1 and should aid in the understanding of the key intrinsic properties of this transporter. Moreover, they appear as good candidates for general blocking activity on the entire EAATs family.

EXPERIMENTAL PROCEDURES

Expression of EAAT1 in Oocytes—Capped RNA was transcribed from linearized pBluescript II SK(−) phagemid vector (Stratagene) containing the coding region for EAAT1 (9, 12) using T3 polymerase (Stratagene). 50 ng of RNA were injected into stage V–VI defolliculated oocytes. L-[14C]Glutamate uptake measurements were made 24 h after injection, whereas electrophysiological recordings were made 2–4 days after injection. From electrophysiological data there was no evidence that the blockers tested had a greater or lesser effect at varying postinjection time.

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L-[14C]Glutamate Uptake Measurements in Oocytes—Uptake was measured in control (injected with water) oocytes and in oocytes expressing bovine EAAT1 during a 20-min incubation in ND96 buffer (96 mM NaCl, 2 mM KCl, 1.8 mM CaCl₂, 1 mM MgCl₂, 5 mM HEPES, pH 7.4) containing 1 μM L-[14C]glutamate (NEN Life Science Products), with or without inhibitors. After washing oocytes three times in ND96 at 4 °C, they were homogenized, and the incorporated radioactivity was counted in a Beckman scintillation counter.

Electrophysiology—Two-electrode voltage-clamp recordings were made with an Axon Instruments Axonom2+B amplifier interfaced to a PC computer running the Pclamp software. Currents were filtered at 10 Hz with an 8-pole Bessel filter (Cyberamp 320, Axon Instruments Inc.) and digitized at 100 Hz. Oocytes were clamped at -70 mV and continuously superfused with ND96 or solutions containing test compounds at various concentrations, flowing by gravity from one of several reservoirs. Switching from one reservoir to another was made with Isolatch Teflon valves (General Valve Corporation) under computer control.

A number of pharmacological agents were tested at a concentration of 100 μM on bovine and human EAAT1. The current elicited is given relative to the one obtained with 100 μM L-glutamate in the same cells. Mean ± S.D. have been obtained from separate measurements in three to five different oocytes.

The currents obtained with various concentrations of substrates on bovine EAAT1 were expressed relative to the maximal current obtained with L-glutamate in the same cells, and the normalized mean concentration response of currents from three cells was fitted by least squares to the equation I = I_max(substrate)/[substrate] + K_s. The block of bovine EAAT1 by DL-threo-β-benzoyloxyaspartate and DL-threo-β-(1-naphthyl)oxyaspartate was evaluated by Schild analysis (33).

Pharmacological Agents—L-Glutamate was from Nacalai Tesque; DL-THA was from Sigma; l- and n-THA were from Toeris. The derivatives of hydroxyaspartate were obtained from the reaction of (2S,3S)*-N-t tert-butoxycarbonyl-3-hydroxyaspartic acid di-tert-butyl ester with the corresponding acyl chloride, followed by deprotection with trifluoroacetic acid. All new compounds were characterized by NMR and are of greater than 95% purity. Full details of the synthesis will be reported elsewhere.

Stock solutions (100 mM) of the commercially available pharmacological agents were made in 0.1 N NaOH and stored at 20 °C. Stock solutions of the synthesized derivatives of DL-THA were made in 50% or 100% dimethyl sulfoxide and stored at 20 °C for months without loss of activity. At thawing, moderate warming and vortexing was necessary to achieve a clear solution, which was then diluted as needed in ND96. The final concentration in dimethyl sulfoxide (0.3% maximum) had no effect on I\textsubscript{EAAT1}.

RESULTS

A series of derivatives of the glutamate transporters substrate DL-threo-β-hydroxyaspartate were synthesized and tested for their ability to inhibit L-[14C]glutamate uptake and glutamate-induced I\textsubscript{EAAT1} in Xenopus oocytes injected with cRNA encoding bovine excitatory amino acid transporter EAAT1 (Fig. 1). Uptake of 1 μM L-[14C]glutamate into oocytes injected with cRNA expressing bovine EAAT1 was linear for more than 30 min and was increased 10–20 times over control (injected with water) oocytes. Addition of l-THA, DL-THA, D-THA, DL-threo-β-acetoxyspartate (DL-TPnOAsp), DL-threo-β-propionyloxyaspartate (DL-TBzO-Asp), DL-threo-β-(1-naphthyl)oxyaspartate (DL-T1NpOAsp), DL-threo-β-(2-naphthyl)oxyaspartate (DL-T2NpOAsp) (100 μM) resulted in a marked decrease in L-[14C]glutamate uptake (Fig. 2). The five new THA derivatives produced 65–85% inhibition of L-[14C]glutamate uptake. In contrast, kainate, a well-known blocker of EAAT2 (12), produced only a weak inhibition of L-[14C]glutamate uptake by bovine EAAT1 (not shown), in agreement with previously published results on human EAAT (12).

The mechanism underlying the inhibition of glutamate transport by THA derivatives was investigated by electrophysiology. DL-THA derivative-mediated inhibition was due to specific interaction with the transporters, as their application did not induce a current in un.injected oocytes, nor were the currents induced by L-glutamate on injected oocytes altered by co-application of the vehicle (up to 0.3% dimethyl sulfoxide) with glutamate (not shown).

To determine whether or not some of the THA derivatives could be blockers, we checked the electrogenicity of these compounds onto voltage clamped oocytes expressing bovine EAAT1. Superfusion of voltage-clamped oocytes expressing bovine EAAT1 with THA, DL-TAcOAsp or DL-TBzOAsp (100 μM) elicited transport current (n = 5 from two different batches of oocytes, Fig. 3, A and C). In contrast, superfusion with DL-TBzOAsp, DL-T1NpOAsp, or DL-T2NpOAsp (100 μM) did not induce a detectable current (n = 3–5 from two different batches of oocytes; Fig. 3, B and C). However, the glutamate induced I\textsubscript{EAAT1} was significantly reduced in the presence of these last three THA derivatives (Fig. 3, B and C), in agreement with the inhibitory activity of these compounds on L-[14C]glutamate uptake in oocytes expressing bovine EAAT1 (Fig. 2).

The kinetic parameters of l-THA, DL-TAcOAsp, and DL-TPnOAsp were determined by measuring the concentration dependence of the uptake current, as illustrated for DL-TPnOAsp (Fig. 4A). l-THA, DL-TAcOAsp, and DL-TPnOAsp elicited dose-dependent and saturable transport currents, the maximum value of which (I\textsubscript{max}) was normalized to the maximum current obtained with L-glutamate in the same oocytes. The kinetic parameters obtained are listed in Table I. The values are expressed as mean ± S.D. from at least three cells. l-THA was tested on only two oocytes.

The mechanism of DL-TBzOAsp and DL-T1NpOAsp inhibition on glutamate transport was examined by studying the effect of different concentrations of these compounds on the kinetic parameters for the glutamate induced I\textsubscript{EAAT1}. The apparent
affinity for l-glutamate was shifted from 19 ± 3 μM to 56 ± 6 μM and to 117 ± 18 μM in the presence of 30 and 100 μM of DL-TBzOAsp, respectively, without a significant modification of the maximal current (Fig. 4B). A similar parallel shift of the dose response curve was obtained for DL-T1NpOAsp, with an apparent affinity for glutamate of 65 ± 5 μM (n = 4) and 118 ± 7 μM (n = 3) in the presence of 100 μM and 300 μM DL-T1NpOAsp, respectively. This parallel shift of the dose response curve for glutamate demonstrates that DL-TBzOAsp and DL-T1NpOAsp are competitive blockers of bovine EAAT1. To determine the antagonism equilibrium dissociation constant (Kᵦ) of DL-TBzOAsp and DL-T1NpOAsp, the agonist dose ratio (r) was calculated at each blocker concentration, and log(r − 1) was plotted against log([blocker]). A linear fit to the data with a slope of 1 allowed to estimate Kᵦ as 17.2 μM for DL-TBzOAsp and 52.1 μM for DL-T1NpOAsp (Table I). The limited amounts of DL-T2NpOAsp available were not sufficient to access the Kᵦ of this compound.

As bovine EAAT1 differs from the human EAAT1 by 12 amino acid residues, we further tested four of our derivatives on the human EAAT1, obtained by polymerase chain reaction cloning after the sequence published by Arriza et al. (12), and expressed in the oocyte system. Similarly to their effect on the bovine EAAT1, DL-TAcOAsp and DL-TPnOAsp were proved to be substrates of the human EAAT1, whereas DL-TBzOAsp and DL-T1NpOAsp were not electrogenic when applied alone, but able to inhibit the current elicited by l-glutamate. Currents elicited by 100 μM DL-TAcOAsp and DL-TPnOAsp had, respectively, an amplitude of 31 ± 2% and 2.5 ± 0.5% relative to that obtained with 100 μM glutamate in the same oocytes (n = 4).

When co-applied with 100 μM l-glutamate, 100 μM DL-TBzOAsp and DL-T1NpOAsp inhibited the glutamate-induced current by 54 ± 5% and 25 ± 5%, respectively (n = 4).

**DISCUSSION**

Recent attempts to develop EAATs inhibitors were done having in mind to obtain structural data on the pharmacopore of the transporters. A number of conformationally restrained analogues of glutamate have been designed for this purpose (20–22). The blocking activity of kainate and dihydrokainate on EAAT2 (12) demonstrates that such developments should be successful, but also indicates that, most probably, selective, rather than general, blockers should arise from such work. In our attempts to develop general blockers for EAATs, we started from the structure of the well known general substrate, DL-THA, which is quite flexible, and increased the steric hindrance without making any attempt to restrict the conformational dynamics of the molecule. It is noteworthy that kainate is a selective blocker of EAAT2, whereas 1-trans-pyrrolidine-2,4-dicarboxylic acid, which contains a more extended embedded glutamate-like conformation (21), is a general substrate (12). On the other hand, it has been shown that there is an inverse relationship between steric bulk at the 4-position and transport inhibition in the kainate-like derivatives: 1-trans-2,3-homo-pyrrolidine-2,4-dicarboxylic acid, which has a hydrogen in that

**FIG. 3. Potency of THA and its derivatives to induce IEAAT1, and to inhibit the glutamate-induced current into oocytes expressing bovine EAAT1.** A, application of 100 μM of THA or the derivatives DL-TAcOAsp and DL-TPnOAsp induce an inward current. B, application of the derivatives (100 μM) DL-TBzOAsp, DL-T1NpOAsp, and DL-T2NpOAsp gives no detectable current (left) but co-application of these derivatives with l-glutamate inhibits the glutamate-induced IEAAT1 (right). C, the results are expressed relative to the current obtained with 100 μM l-glutamate in the same cells. Each column represents mean ± S.D. (n = 4–6). DL-TBzOAsp, DL-T1NpOAsp, and DL-T2NpOAsp gave no detectable current (n = 3–5). The inhibition of l-glutamate (100 μM)-induced IEAAT1 by these three derivatives was obtained in co-application experiments as illustrated in B.

**FIG. 4. Determination of the kinetic mechanism underlying the inhibition of glutamate transport by THA derivatives.** A, THA; DL-TAcOAsp and DL-TPnOAsp are substrates of bovine EAAT1 as illustrated for DL-TpOAsp. The recordings shown have been obtained with the indicated concentrations of l-glutamate and of DL-TPnOAsp, applied separately onto the same cell. The results were normalized to the maximal current obtained with l-glutamate in each oocyte and mean ± S.D. (n = 3) for l-glutamate (circles) and DL-TPnOAsp (squares) plotted as a function of substrate concentration on a logarithmic scale. The solid line through the data are from the equation $I = I_{\text{max}} \left( \frac{[\text{substrate}]}{K_{\text{m}} + [\text{substrate}] } \right)$. B, DL-TBzOAsp is a competitive blocker of bovine EAAT1. The recordings shown were obtained with the indicated concentrations of l-glutamate and of DL-TpOAsp, applied separately onto the same cell. The apparent affinity of l-glutamate was shifted from 19 ± 3 μM (circles; n = 6) to 56 ± 8 μM in the presence of 30 μM of DL-TBzOAsp (squares, one oocyte, three applications per dose) and to 117 ± 18 μM in the presence of 100 μM DL-TBzOAsp (triangles, n = 3–6 from three different batches) without significant modification of the maximal current.

**TABLE I**

| Substrates | l-Glutamate | l-THA | DL-TAcOAsp | DL-TPnOAsp | DL-TBzOAsp | DL-T1NpOAsp |
|------------|-------------|-------|-------------|-------------|-------------|-------------|
| $K_a$ (μM) | 19 ± 3      | 0     | 40 ± 11     | 64 ± 9      | 17.2*       | 52.1*       |
| $I_{\text{max}}$ | 1           | 0.68  | 0.55 ± 0.01 | 0.12 ± 0.01 | 0           | 0           |

* Determined by Shild analysis; DL-TBzOAsp and DL-T1NpOAsp did not induce currents.

b $I_{\text{max}}$ is normalized to the l-glutamate $I_{\text{max}}$ in the same oocytes.
position, is less active than kainate (isopropenyl group), itself less active than dihydrokainate (isopropyl group) (12, 21, 34). In this study, we demonstrated that even the THA derivatives possessing bulky groups could fit to the binding site of bovine EAAT1, possibly the result of the flexibility of the molecules. However, some of these derivatives cannot undergo transport, probably because of an interaction between the bulky group and the transporter protein. Such an interaction seems even to favor binding itself, as DL-TBzOAsp has a better affinity for bovine EAAT1 than the least electrogenic of our substrates, DL-TPnOAsp. Further increase of the steric hindrance nevertheless lowers the affinity, as shown by the weaker activity of DL-T1NpOAsp and DL-T2NpOAsp, compared with DL-TBzOAsp.

The results presented in this study are so far concerned with only the EAAT1 subtype of EAATs. Preliminary results on the activity of DL-TBzOAsp on a new member of the EAAT2 subtype we recently cloned from human brain indicate that this compound is also a blocker of this subtype, with even a better affinity than for bovine EAAT1 (results will be published elsewhere).

We cannot rule out the possibility that our nonelectrogenic derivatives are indeed transported in a nonelectrogenic manner. The only definite experiment that could address this possibility would be an uptake assay of radiolabeled derivatives, which we could not synthesize. Nevertheless, the fact that our series of derivatives comprises substrates of decreasing electrogenicity argues well against the hypothesis of a nonelectrogenic transport process.

Excitatory amino acid transporters are known to possess a substrate-gated chloride conductance that is thermodynamically independent of the electrogenic transport of substrates (14, 27, 32, 35). The transporter subtypes differ in the magnitude of this chloride flux relative to flux of glutamate (27). A substrate-independent monovalent cation conductance has also been demonstrated in the human astroglial transporter EAAT1, whereas it is absent in EAAT2 (28). This latter conductance was evidenced by the fact that oocytes expressing EAAT1 had an increased conductance, compared with oocytes expressing EAAT2 or control oocytes. The sensitivity to kainate was transferred to EAAT1 by constructing a chimera transporter comprising part of the substrate binding site of EAAT2. The superfusion of kainate on oocytes expressing the chimeric transporter induced an apparent outward current, revealing the inward leak conductance. In contrast, in this study, the superfusion of DL-TBzOAsp, DL-T1NpOAsp, or DL-T2NpOAsp on oocytes expressing bovine or human EAAT1 did not induce a detectable current. This result suggests that the ions that carry the uncoupled current are unlikely to permeate the same pore region of the transporter than that of the substrates. The striking differences in the action of our derivatives compared with kainate suggest that these blockers have different mechanisms of action. The leak conductance blockade by kainate to the blockade of the leak conductance in the EAAT1/EAAT2 chimera. As preliminary results indicate that our derivatives also block EAAT2, it would be interesting to test whether or not they would block the leak conductance of the EAAT1/EAAT2 chimera.

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REFERENCES
1. Balcar, V. J., and Johnston, G. A. (1972) J. Neurochem. 19, 2657–2666
2. Kanner, B. I., and Sharon, I. (1978) Biochemistry 17, 3949–3953
3. Zerangue, N., and Kavanaugh, M. P. (1996) Nature 385, 634–637
4. Storek, T., Schulte, S., Hofmann, K., and Stoffel, W. (1992) Proc. Natl. Acad. Sci. U. S. A. 89, 10955–10959
5. Tanaka, K. (1993) Neurosci. Res. 16, 149–153
6. Tanaka, K. (1993) Neurosci. Res. 16, 183–186
7. Pines, G., Danbolt, N. C., Bjorjs, M., Zhang, Y., Bendahan, A., Eide, L., Koopsel, H., Storm-Mathisens, J., Seeberg, E., and Kanner, B. I. (1992) Nature 360, 464–467
8. Kanai, Y., and Hediger, M. A. (1992) Nature 360, 467–471
9. Inoue, K., Sakaitani, M., Shimada, S., and Tohyama, M. (1995) Mol. Brain Res. 28, 343–346
10. Shashidharan, P., and Paltakis A. (1993) Biochim. Biophys. Acta 1216, 161–164
11. Kawakami, H., Tanaka, K., Nakayama, T., Inoue, K., and Nakamura, S. (1994) Biochem. Biophys. Res. Commun. 199, 171–176
12. Arriza, J. L., Fairman, W. A., Dadiche, J. I., Muroch, G. H., Kavanaugh, M. P., and Amara, S. G. (1994) J. Neurosci. 14, 5559–5569
13. Shashidharan, P., Wittenberg, I., and Paltakis A. (1994) Biochim. Biophys. Acta 1191, 393–396
14. Fairman, W. A., Vandenberg, R. J., Arriza, J. L., Kavanaugh, M. P., and Amara, S. G. (1995) Nature 375, 599–603
15. Rothstein, J. D., Martin, L., Levey, A. I., Dykes-Hoberg, M., Jin, L., Wu, D., Nash, N., and Kunc, R. W. (1994) Neuron 13, 713–725
16. Rothstein, J. D., Van Kammem, M., Levey, A. I., Martin, L., and Kunc, R. W. (1995) Ann. Neurol. 38, 73–84
17. Lehre, K. P., Levy, L. M., Ottersen, O. P., Storm-Mathisens, J., and Danbolt, N. C. (1995) J. Neurosci. 15, 1835–1853
18. Rothstein, J. D., Dykes-Hoberg, M., Parais, C. A., Bristol, L. A., Jin, L., Kunc, R. W., Kanay, Y., Hediger, M. A., Wang, Y., Schieleke, J. P., and Welty, D. F. (1996) Neuron 16, 675–686
19. Tanaka, K. (1993) J. Neurosci. Res. 16, 491–503
20. Bridges, R. J., Lovering, F. E., Humphrey, J. M., Martin, L. S., Christofaro, M. F., and Chamberlin, A. R. (1993) Bioorg. Med. Chem. Lett. 3, 115–121
21. Bridges, R. J., Lovering, F. E., Koch, H., Cotman, C. W., and Chamberlin, A. R. (1994) Neurosci. Lett. 174, 193–197
22. Brew, H., and Attwell, D. (1987) Nature 327, 707–709
23. Barbou, B., Brew, H., and Attwell, D. (1988) Nature 335, 433–435
24. Barbou, B., Brew, H., and Attwell, D. (1991) J. Physiol. 436, 169–193
25. Klockner, U., Storek, T., Conrad, M., and Stoffel, W. (1995) J. Biol. Chem. 268, 14594–14596
26. Wadiche, J. I., Arriza, J. L., Amara, S. G., and Kavanaugh, M. P. (1995) Neuron 14, 1019–1027
27. Vandenberg, R. J., Arriza, J. L., Amara, S. G., and Kavanaugh, M. P. (1995) J. Biol. Chem. 270, 17668–17671
28. Klockner, U., Storek, T., Conrad, M., and Stoffel, W. J. (1994) J. Neurosci. 14, 5759–5765
29. Grant, G. B. (1992) Characterization and Function of the Electrogenic Glutamate Transporter in Rod Photoreceptors of the Tiger Salamander Retina. Ph.D. dissertation, University of California, Berkeley
30. Picard, S. A., Larsson, H. P., Wells, D. P., Lecar, H., and Werblin, F. S. (1995) Proc. Natl. Acad. Sci. U. S. A. 92, 9417–9421
31. Larsson, H. P., Picard, S. A., Werblin, F. S., and Lecar, H. (1996) Biochim. J. 370, 733–742
32. Arunlakshana, O., and Schild, H. O. (1959) Br. J. Pharmacol. 14, 48–58
33. Sonnenberg, J. D., Koch, H., Willis, C. L., Bradbury, F., Dauerhauer, D., Bridges, and Chamberlin, A. R. (1996) Bioorg. Med. Chem. Lett. 6, 1607–1612
34. Billups, B., Rossi, D., and Atwell, D. (1996) J. Neurosci. 16, 6722–6731
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