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Evaluation of a novel glass vial overcoming adsorption effect for pharmaceutical drugs

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Introduction

The majority of pharmaceutical drugs are still small molecule drugs. Many of them consist of basic compounds. Although carryover is one of the biggest issues when analyzing basic compounds with HPLC, the recent progress of HPLC system has been overcoming the issue. On the one hand, adsorption onto consumables when in sample preparation is regarded as another big issue. Especially, adsorption onto vials directly decreases the accuracy and the precision of quantitative values. Two main materials of HPLC vial are glass and polypropylene.

It is famous that basic compounds adsorb to glass surface and hydrophobic compounds absorb to polypropylene surface, respectively. The adsorption rate elevates at the lower sample concentration. Thus, recent progress of HPLC system on sensitivity emphasize the adsorption effect. To overcome the adsorption effect, we developed and evaluated a novel glass vial "LabTotal vial" which is highly inert to basic compounds and perfect for highly sensitive LC/MS analyses.

Methods

Regent and standards

Reagents : Standard samples (amitriptyline, atenolol, imipramine and propranolol) and TFA were purchased from Wako chemical. Water was made in house using a Millipore Milli-Q Integral 5 Ultrapure Water Purification System. Acetonitrile and methanol were purchased from Nacalai tesque.
Standard solutions : Stock solutions were prepared by dissolving 0.1 mg of standard samples in 100 mL of water, respectively. They were diluted in mobile phase before use.

Analytical conditions

LC System : Nexera MP system (Shimadzu corporation)
Detector : SPD-M30A photodiode array detector and LCMS-8060 triple quadrupole mass spectrometer
Surface analyzer : Nano search microscope SFT-4500 (Shimadzu corporation)

Table 1 LC and LC/MS/MS Analytical Conditions

Column	: Shim-pack XR-ODS seris columns (100 mm L. x 2.0 mm I.D./50 mm L. x 2.0 mm I.D., 2.2 µm)
Mobile Phase	: A: 0.1 % TFA in water; B: 0.1 % TFA in Acetonitrile 40%B (Amitriptyline, Imipramine), 20%B (Propranolol), 10%B (Atenolol)
Flow Rate	: 0.5 mL/min
Column Temperature	: 40 °C
Injection Volume	: 1 µL
Detection	: 254 nm (Amitriptyline, Imipramine), 280 nm (Atenolol), 290 nm (Propranolol), 240 nm (Amiodarone), ESI-positive MRM mode (Figure 3)

Results

Comparison of adsorption of basic compounds

The novel glass vial "LabTotal Vial" and other vendor's vials were evaluated for adsorption of four basic compounds. The LabTotal vial showed the highest inertness for all compounds.

Table 2 Peak area and estimated recovery rate

Compound	1 mg/L Amitriptyline	1 mg/L Atenolol	1 mg/L Imipramine	1 mg/L Propranolol
LabTotal Vial	51376 (100%)	8638 (100%)	64990 (100%)	32249 (100%)
Vendor A (for LCMS)	45376 (88%)	7620 (88%)	55531 (85%)	31496 (97%)
Vendor B (for LC/GC)	21788 (42%)	6137 (71%)	24131 (37%)	27327 (84%)

*Recovery rate was estimated by divided by the peak area of LabTotal vial.

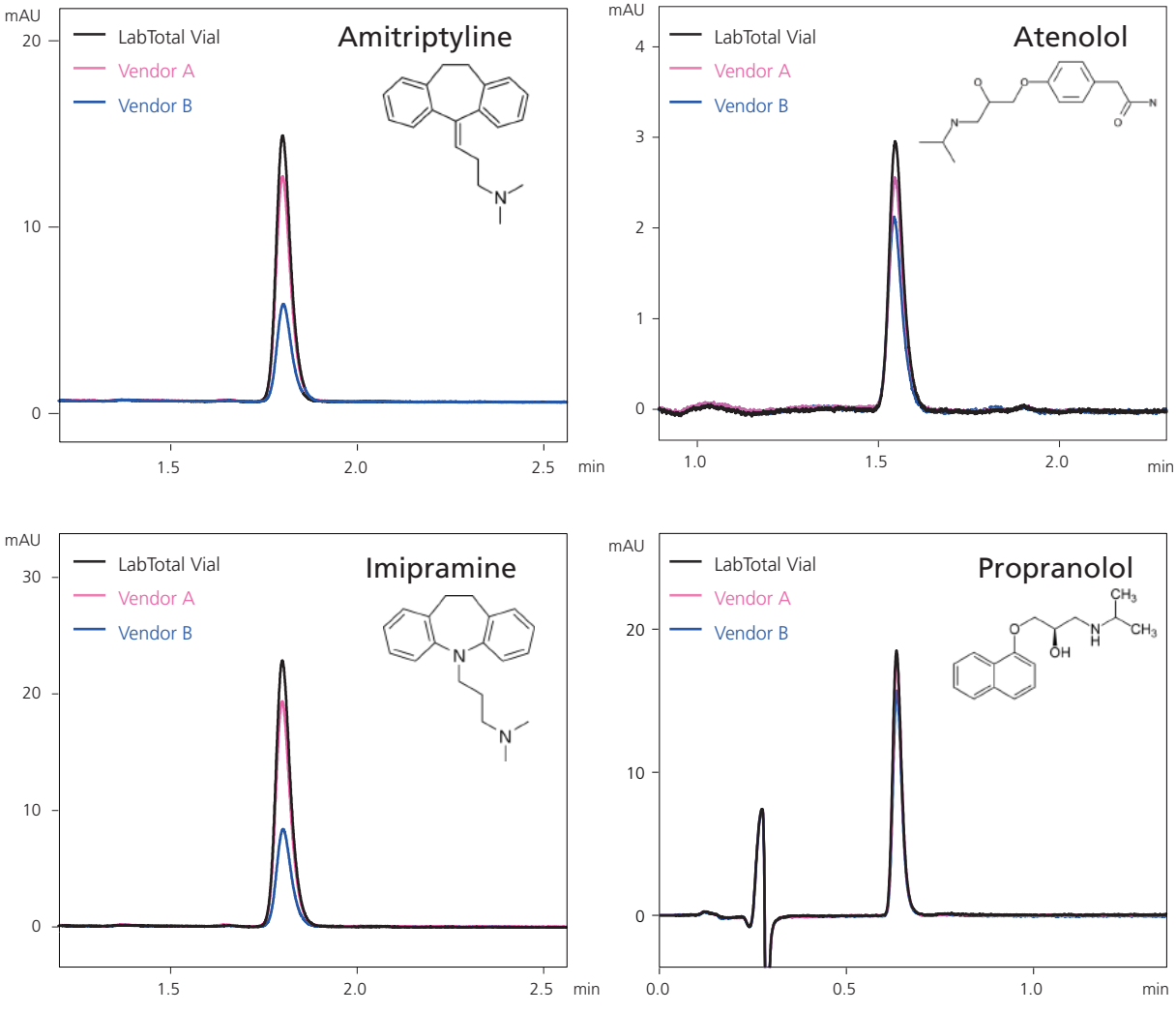

Figure 1 Structures and chromatograms of four basic compounds

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Adsorption effect on ultratrace analysis

To evaluate the performance for trace analysis with LC/MS/MS, the LabTotal vial and the vendor A vial (for LC/MS) were tested with 0.05 µg/L basic compound solution. The LabTotal vial showed about 2 times higher peak area than the vendor A vial.

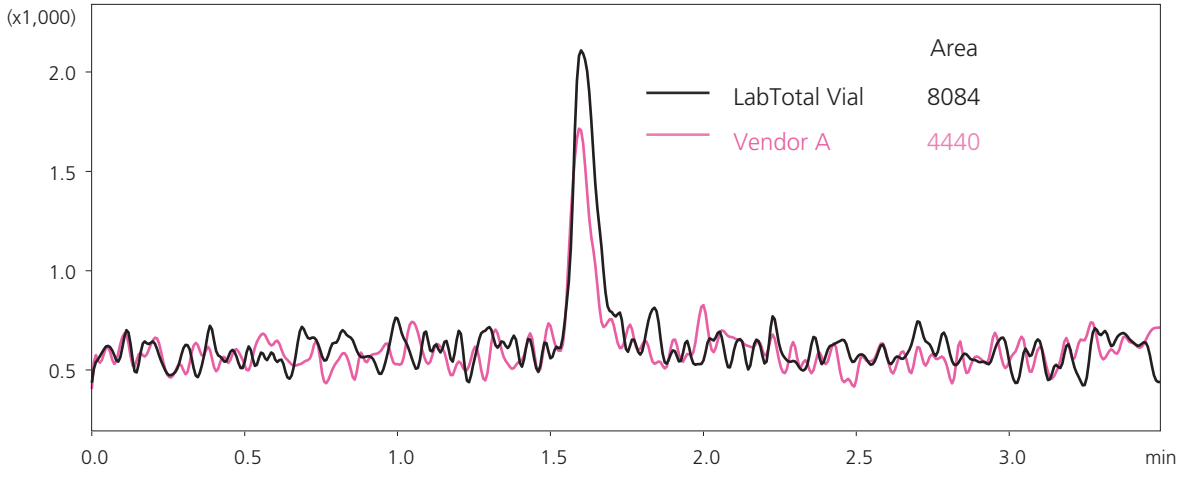

Fig.3 MRM Chromatogram of 0.05 µg/L Basic Compound Standard Solution

Adsorption effect for the compounds having both basic and hydrophobic properties

Amiodarone is a compound having both hydrophobic and basic properties and adsorbs onto both glass and polypropylene vials. The LabTotal vial showed excellent inertness far more than both vials. The data suggested that the LabTotal vial is suit for the compounds which have various properties or unknown property.

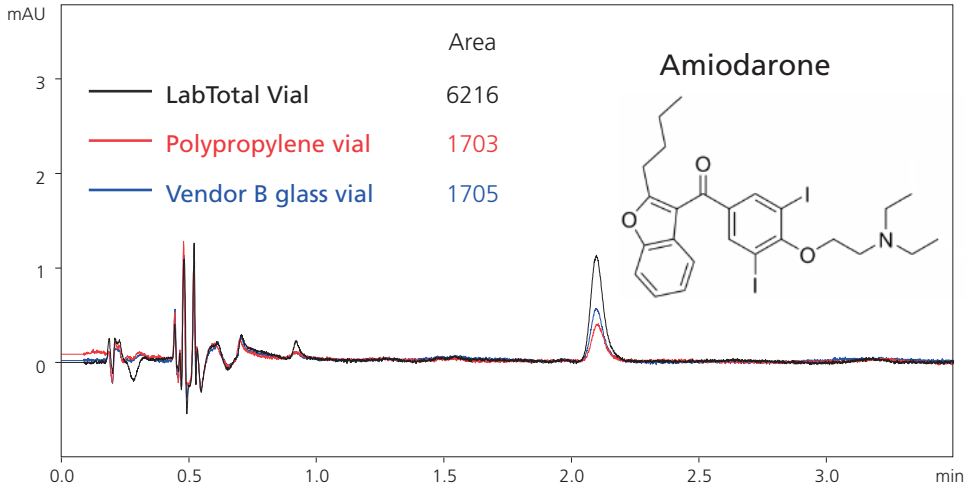

Fig.4 Structure and chromatograms of Amiodarone (1 mg/L)

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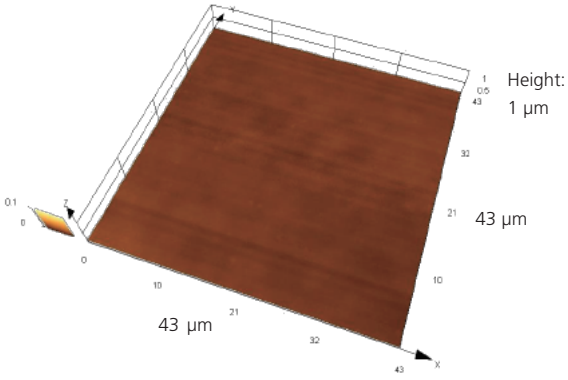
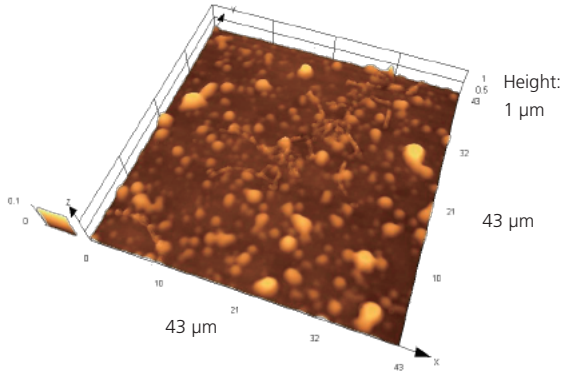
Analysis of glass surface

To understand the causes of the higher inertness of the LabTotal vial, its microstructure was compared with vendor B vial. The LabTotal vial has quite smooth surface structure by contrast with vendor B vial having rough structure. Furthermore, by analyzing their nanostructures, hole structures were found on the latter vial. The hole size was reasonable to trap small compounds and then explain the cause of the higher adsorption effect.

LSM Height image (3D)



LSM Height image (3D)



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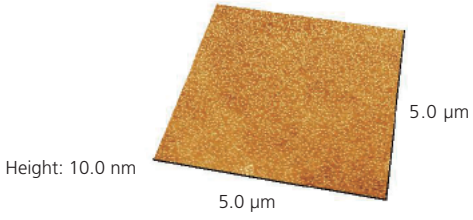

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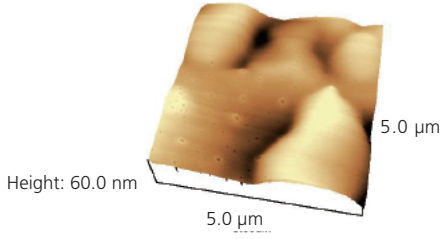

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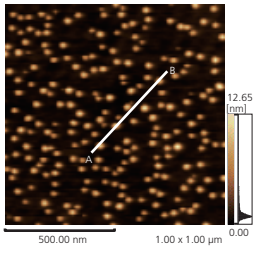
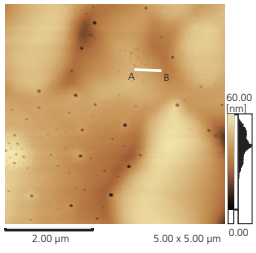
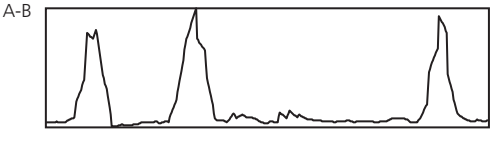


AFM Height image (2D)



Shape profile



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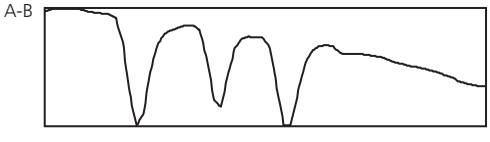

Fig.5 Surface analysis of LabTotal Vial

Fig.6 Surface analysis of Vendor B's Vial

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Conclusions

- The LabTotal vial showed the higher inertness for not only basic compound but also the compound having both basic and hydrophobic properties.
- The LabTotal vial also showed the excellent performance for very low amount of sample. Thus, it is preferable for trace analysis using LC/MS/MS.
- The smooth micro/nano structure of the LabTotal vial is supporsed to cause its lower adsorption activity.
- The evaluation results demonstrated that the LabTotal Vial can be a first choice regardless of the properties of the target compound. Especially, it is quite effective to the unknown samples requiring the highly precise quantitative results and the multicomponent samples having various properties.

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