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Morphology Effect of Bismuth Vanadate on Electrochemical Sensing for the Detection of Paracetamol

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Abstract: Morphology-control, as a promising and effective strategy, is widely implemented to change surface atomic active sites and thus enhance the intrinsic electrocatalytic activity and selectivity. As a typical n-type semiconductor, a series of bismuth vanadate samples with tunable morphologies of clavate, fusiform, flowered, bulky, and nanoparticles were prepared to investigate the morphology effect. Among all the synthesized samples, the clavate shaped BiVO$_4$ with high index facets of (112), (301), and (200) exhibited reduced extrinsic pseudocapacitance and enhanced redox response, which is beneficial for tackling the sluggish voltammetric response of the traditional nanoparticle on the electrode surface. Benefiting from the large surface-active area and favorable ion diffusion channels, the clavate shaped BiVO$_4$ exhibited the best electrochemical sensing performance for paracetamol with a linear response in the range of 0.5–100 µmol and a low detection limit of 0.2 µmol.

The enhanced electrochemical detection of paracetamol by bismuth vanadate nanomaterials with controllable shapes indicates their potential for applications as electrochemical sensors.

Keywords: BiVO$_4$; morphology control; electrochemical sensor; paracetamol

1. Introduction

Drug detection is essential in the monitoring of drug molecules in bio-fluids and plays an important role in drug quality control [1,2]. Paracetamol, also known as acetaminophen, is one of the most popular analgesics/antipyretics and has been applied in effective treatment of pain and fever in adults and children [3,4]. Paracetamol distributes rapidly after oral administration and is easily excreted in the urine. Unlike other analgesic drugs, paracetamol does not produce gastrointestinal damage or untoward cardiorenal effects [5,6]. However, the hypersensitivity or overdose of paracetamol can lead to formation of some liver and nephrotoxic metabolites, such as acute liver necrosis [7]. Moreover, the hydrolytic degradation product of paracetamol is 4-amino-phenol that can be found in pharmaceutical preparations and can cause teratogenic effect and nephrotoxicity [8].

It is desirable to develop an efficient electrochemical catalyst for paracetamol for the quality control of pharmaceuticals, physiological function, and diagnosis in clinical medicine [9]. Semiconductors have been taken as effective photocatalytic and electrochemical sensors for direct detection of paracetamol [10–13]. Therein, transition metal oxide BiVO$_4$, with an excellent charge transport property (hole diffusion length $L_p = 70$ nm) [14,15], has emerged as a highly promising electrocatalytic material with good chemical stability, environmental inertness, and low cost [16,17]. Medeiros et al. reported that BiVO$_4$ nanoparticles could be used as a highly efficient and sensitive photoelectrochemical sensor for paracetamol detection [18]. Generally speaking, morphology optimization can further enhance the electrocatalytic performance of material oxides. Control of the size and shape of material oxides is essential to optimize their active areas and favorable ion diffusion channels [19]. As a result, many efforts have been made to engineer metal oxides on the nanoscale that have led to the understanding of their fundamental size- and
shape-dependent properties [20]. For example, porous BiVO$_4$ with a larger surface area and more reactive sites compared with nanoparticle shape could afford a faster electron transfer rate, as well as higher stability and reproducibility of the sensor [21]. The ability to control the particle morphology can provide a means to tune so-called structure-sensitive catalytic reactions [22,23]. It is highly desirable to be able to synthesize electrocatalytic materials with different morphologies in a facile and controllable manner for the purpose of improving the sensitivity of paracetamol detection, as well as investigating the morphology effect on the electrochemical sensing.

In this work, the BiVO$_4$ electrodes with different morphologies were prepared for the purpose of investigating the influence of morphology on sensitivity of electrochemical sensing. The BiVO$_4$ samples were synthesized by the microwave approach at 180 °C for 30 min. The addition of additives and the adjustment of the pH value of solutions could change the morphology of the BiVO$_4$ samples effectively. Further, the influence of different morphology of BiVO$_4$ on the electrochemical detection of paracetamol was explored. Among all synthesized BiVO$_4$ samples, the clavate morphological of the BiVO$_4$ electrode exhibited the best electrochemical sensing performance on paracetamol with the widest linear detection range (0.5–100 µM) and lowest detection limit (0.2 µM).

2. Experimental Section

2.1. Apparatus

A microwave chemistry working platform (Model: TOPEX+, PreeKem Scientific Instruments Co., Ltd., Shanghai, China) and high-performance liquid chromatography (Model: Essentia CTO-16L, Shimadzu, Shanghai, China) were used. Scanning electron microscopy (SEM) images were obtained by Apreo (Thermo Scientific, Waltham, MA, USA). Field emission transmission electron microscopy (TEM) images were recorded using a TecnaiTM G2 F30 (FEI Co. Ltd., Hillsboro, OA, USA). X-ray diffraction (XRD) characterization was carried out on a D2 PHASER (Bruker, Karlsruhe, Germany) with Cu-Kα as the radiation source (λ = 0.154 nm). X-ray photoelectron spectroscopy (XPS, K-Alpha+, Thermo Scientific, MA, USA) was used. The C1s binding energy of adventitious carbon contamination with 284.6 eV was selected as the reference. UV–Vis diffuse reflectance spectra were recorded with a UV–Vis spectrophotometer (Model: Frontier, PerkinElmer Inc., MA, USA). All the electrochemical experiments were carried out using an electrochemical workstation (CH Instrument 660E, Shanghai Chenhua Instrument Co., Ltd., Shanghai, China). The electrochemical experiment was performed using a conventional three-electrode system with the prepared BiVO$_4$ as the working electrode, a graphite rod as the counter electrode, and a saturated Ag/AgCl electrode as the reference electrode.

2.2. Chemicals and Reagents

Bi(NO$_3$)$_3$.5H$_2$O (99.0%), NH$_4$VO$_3$ (99.9%), KCl (99.8%), NaH$_2$PO$_4$ (99.0%), Na$_2$HPO$_4$ (99.0%), and Na$_2$PO$_4$ (96%) were obtained from Aladdin Reagent (Shanghai) Co., Ltd., Shanghai, China. HCl, Na$_2$CO$_3$ (99.5%), and NaOH (97%) were purchased from Macklin (Shanghai) Biochemical Technology Co., Ltd., Shanghai, China. The standard drug of paracetamol tablets (over the counter, OTC) was obtained from Taiji Pharmaceutical Industrial Co., Ltd., Sichuan, China. Phosphate buffered saline (PBS) was prepared (lab temperature at 26 ± 2 °C) by 0.010 M NaH$_2$PO$_4$, 0.010 M Na$_2$HPO$_4$, and 0.050 M KCl. All solutions were prepared using ultra-pure water supplied by a Milli-Q system (Millipore, Burlington, MA, USA) with a resistivity of 18.2 MΩ cm.

2.3. Preparation of Bismuth Vanadate

The amounts of 5 mM Bi(NO$_3$)$_3$ and 5 mM NH$_4$VO$_3$ were dissolved in 10 mL ultra-pure water. Different amounts of NaH$_2$PO$_4$, Na$_2$HPO$_4$, Na$_2$PO$_4$, and Na$_2$CO$_3$ were used as additives. The amount of 1.0 M NaOH and 36% HCl solutions were used to adjust the pH values of solutions. Then 20 mL amounts of prepared solutions with different pH
values were transferred to 100 mL Teflon reactors. The microwave reaction was carried out at 180 °C for 30 min. Different morphologies of BiVO₄ powders were collected by centrifugation at 12,000 rpm and dried in an oven at 80 °C for 24 h. The BiVO₄ electrodes with different morphologies were prepared by the spin coating method; 5 mg BiVO₄ powder was dispersed in 1 mL DI water by ultrasound for 10 min. Then the BiVO₄ suspension was transferred to FTO substrates by spin coating. The as-prepared BiVO₄/FTO electrodes were annealed in a muffle furnace with 200 °C for 2 h for stabilization. Finally, the BiVO₄/FTO electrodes with different morphologies were obtained.

2.4. Determination of Paracetamol in Tablets

High performance liquid chromatography (HPLC) was used for the estimation of the content of paracetamol in standard drug of paracetamol tablets. The method was carried out on a Hichrom C18 (25 cm × 4.6 mm i.d., 5 µm) column with a mobile phase consisting of methanol and icy ultra-pure water containing formic acid (volume ratio of 50%/49.9%/0.1%) at a flow rate of 0.2 mL min⁻¹. Detection was carried out at 257 nm. Standard stock solutions of 0, 10, 20, 50, and 100 µmol of paracetamol were prepared in PBS (pH = 7.4), respectively. The injection volume of solution was 50 µL.

3. Results and Discussion

3.1. Characterization of BiVO₄ with Different Morphologies

The synthesis procedures with different conditions to obtain different morphologies of BiVO₄ are summarized in Figure S1. The morphology of bismuth vanadate could be controlled with different additives, including NaH₂PO₄, Na₂HPO₄, Na₃PO₄, and Na₂CO₃. The pH values of the solutions were adjusted in the range of 2 to 10 with HCl or NaOH. Due to the differences in ionization and hydrolysis of phosphate, carbonate, and alkaline, the morphology of bismuth vanadate could form nanosheet, tetrahedron, cuboid, sphere, or irregular shapes. In this article, several representative morphologies of bismuth vanadate were selected, which were denoted as clavate, fusiform, flowered, bulky, and particle BiVO₄, as illustrated in Figure 1. Certain bismuth vanadate samples were chosen as representatives to discuss the effect of morphology on electrochemical properties of BiVO₄ materials.

Figure 1. SEM images of BiVO₄ with selected morphology: (A) clavate, (B) fusiform, (C) flowered, (D) bulky, and (E) particle. (F) Schematic diagram of shape control of the bismuth vanadate.
The particle BiVO₄ was obtained by adding Na₃PO₄ to the precursor solution (Figure 1E). Then HCl was added drop by drop to adjust the pH value to 4. The Bi³⁺ ions and VO₃⁻ ions combined to form nanoparticles. The size of BiVO₄ nanoparticles ranged from 30 to 300 nm. The clavate and fusiform topography were obtained by adding Na₂HPO₄ (Figure 1A,B). The pH values of solutions were adjusted to 9.5 and 3.6, respectively. The pH value of 0.1 M Na₃HPO₄ solution was about 9 (Ka₁ = 7.1 × 10⁻³). Due to the similar pH values of solution, the clavate morphology BiVO₄ was formed directly and rapidly. By contrast, the fusiform BiVO₄ was formed by the aggregation of nanoparticles (Figure S2), which was due to the partial dissolution and structural reorganization during the process of adjusting the pH value of the solution. The flowered BiVO₄ was formed with the addition of NaH₂PO₄. NaH₂PO₄ solution is acidic (Ka₁ = 6.2 × 10⁻⁸). NaOH was added slowly to change the pH value of solution to 7.7. The BiVO₄ gradually assumed a cross-linked flowered-sphere structure with a diameter of ca. 5 µm (Figure 1C). The bulky topography of BiVO₄ could be obtained by adding NaHCO₃ and adjusting the pH value to 6 (Figure 1D). The bulky BiVO₄ showed a cube structure with a hole in the center.

Due to the different hydrolysis and ionization rates of carbonate and phosphate, the pH values of the solution were different, which further affected the nucleation rate of the Bi⁺ in solution. A further change in the pH of the solution would lead to the dissolution or reshaping of BiVO₄ samples. As a result, the morphology control of BiVO₄ could be achieved with different additives and pH values.

The selected BiVO₄ samples were characterized with a powder X-ray diffractometer (Figure 2A). Bulky BiVO₄ exhibited reflection planes (101), (200), (112), and (312) corresponding to the 2θ values of 18.3°, 24.3°, 32.7°, and 48.4°, respectively. These values are well matched with standard JCPDS file No. 14-0133, illustrating a tetragonal phase of bulky BiVO₄. The clavate BiVO₄ sample exhibited a tetragonal structure. Moreover, diffraction peaks of impurities (Bi₂O₅) were observed in clavate BiVO₄. Particle BiVO₄ exhibited sharp diffraction peaks at 18.6°, 28.6°, and 30.9°, which correspond to (101), (112), and (004) crystal planes, respectively (JCPDS file No. 48-0744). The fusiform morphological sample exhibited (011), (004), and (113) planes of orthorhombic structure as indicated by the 2θ of 19.1°, 29.8°, and 33.1° (JCPDS file No. 12-0293). Notably, there were no clear diffraction peaks in the flowered BiVO₄ sample, indicating poor crystallization of the flowered BiVO₄ sample. Overall, the selected BiVO₄ samples exhibited different properties, which are summarized in Table 1.

The surface chemical states of selected BiVO₄ samples were further investigated by XPS. As for the O 1s spectrum (Figure 2F), the peaks around 529.2 eV were clearly shown in particle, bulky, and flowered BiVO₄ samples, which could be attributed to the lattice oxygen (O²⁻) in BiVO₄ [24]. High-resolution XPS spectra of O 1s after peak fitting were shown in Figure S3. The peak at 529.2 eV was not observed in clavate and fusiform BiVO₄ samples, while a new peak at 530.4 eV appeared, which could be ascribed to the lattice oxygen in bismuth oxide, suggesting the surface of clavate and fusiform BiVO₄ were oxidized. The existence of the surface oxide layer in clavate and fusiform BiVO₄ samples was further confirmed by high-resolution XPS spectra of Bi 4f (Figure 2E) and V 2p (Figure 2D). The Bi 4f of particle, bulky, and flowered BiVO₄ samples showed two characteristic peaks at 164.8 eV and 159.1 eV that were attributed to Bi 4f₅/₂ and Bi 4f₇/₂, respectively. The Bi 4f of clavate and fusiform BiVO₄ samples showed an apparent shift to high binding energy, attributed to the bismuth oxide. A similar phenomenon could be observed in the V 2p spectra. The V 2p peaks were not shown in clavate and fusiform BiVO₄ samples due to the surface oxide layer that covered the single V orbit. XRD results show that the clavate and fusiform BiVO₄, which were both synthesized with Na₂HPO₄, were much more unstable. The VO₄ unit in BiVO₄ easily formed a new bismuth oxide unit as well as oxygen vacancies on the surface of BiVO₄.
The Kubelka–Munk function, and R is the absolute reflectance of the sample. The optical band gap of the prepared samples is calculated using Tauc’s equation: \( F(R) h \nu = A(h \nu - E_g)^n \), where \( n = 2 \) for a directly allowed transition, and \( n = 1/2 \) for an indirectly allowed transition, and \( A \) is a constant and \( h \nu \) is photon energy [25]. According to the calculation, the band gap (\( E_g \)) of the selected BiVO₄ was summarized in Table 1. The band gap of intrinsic BiVO₄ is around 2.4 eV [26]. The particle, bulky, and flowered BiVO₄ showed a comparable value of \( E_g \) with intrinsic BiVO₄, while clavate and fusiform BiVO₄ had a larger value of \( E_g \) due to the surface oxide layer. Generally speaking, BiVO₄ shows excellent photoelectrochemical performance due to its suitable band gap. To investigate the influence of the solar light in photo-assisted detection of paracetamol, differential pulse voltammetry (DPV) of clavate BiVO₄ on determination of paracetamol in the dark and under illumination was studied.

Table 1. Properties of BiVO₄ samples with different morphologies.

| Shape     | Structure  | Size              | Color    | Band Gap | Impurity |
|-----------|------------|-------------------|----------|----------|----------|
| clavate   | tetragonal | \( L = 5 \, \mu m \) \n\( W = 400 \, nm \) | white    | 3.45 eV  | bismuth oxide |
| fusiform  | orthorhombic | \( L = 5-10 \, \mu m \) \n\( W = 2-4 \, \mu m \) | off-white | 3.30 eV  | bismuth oxide |
| flowered  | tetragonal | \( D = 5 \, \mu m \) | light-yellow | 2.38 eV  | None     |
| particle  | tetragonal | \( D = 600 \, nm \) | yellow   | 2.40 eV  | None     |
| bulky     | tetragonal | \( D = 100-200 \, nm \) | yellow   | 2.45 eV  | None     |

\( L = \) length, \( W = \) width, \( D = \) diameter.

3.2. Optical Analysis of BiVO₄ Samples

The BiVO₄ powders obtained from different precursors showed different colors (the inset of Figure 2B). The flowered, bulky, and particle BiVO₄ showed yellow color with the band edge of optical absorption at around 550 nm. The clavate and fusiform BiVO₄ exhibited a white color with a shift of optical absorption edge to about 400 nm (Figure 2B). The change of the color was due to the surface oxide layer of BiVO₄. The UV–vis DRS data were combined with the Kubelka–Munk (K–M) relation to study the association of diffused reflectance with the absorption coefficient: \( F(R) = (1 - R)^2 / 2R \), where \( F(R) \) is the Kubelka–Munk function, and \( R \) is the absolute reflectance of the sample. The optical band gap of the prepared samples is calculated using Tauc’s equation: \( F(R) h \nu = A(h \nu - E_g)^n \), where \( n = 2 \) for a directly allowed transition, and \( n = 1/2 \) for an indirectly allowed transition, and \( A \) is a constant and \( h \nu \) is photon energy [25]. According to the calculation, the band gap (\( E_g \)) of the selected BiVO₄ was summarized in Table 1. The band gap of intrinsic BiVO₄ is around 2.4 eV [26]. The particle, bulky, and flowered BiVO₄ showed a comparable value of \( E_g \) with intrinsic BiVO₄, while clavate and fusiform BiVO₄ had a larger value of \( E_g \) due to the surface oxide layer. Generally speaking, BiVO₄ shows excellent photoelectrochemical performance due to its suitable band gap. To investigate the influence of the solar light in photo-assisted detection of paracetamol, differential pulse voltammetry (DPV) of clavate BiVO₄ on determination of paracetamol in the dark and under illumination was studied.

Figure 2. (A) XRD patterns, (B) UV–Vis spectra, (C) Kubelka–Munk plots of BiVO₄. Inset of (B) is the photographs of clavate, fusiform, flowered, bulky, and particle from 1 to 5. High-resolution XPS spectra of (D) V 2p, (E) Bi 4f, and (F) O 1s of different morphologies BiVO₄.
As displayed in Figure S4, the photoresponse current on BiVO₄ electrode increased from 17.5 to 21.0 mA cm⁻², which indicates that solar light has a positive effect on improving the sensitivity of paracetamol detection.

3.3. Electrochemical Response at Various BiVO₄ Electrodes

Electrochemical techniques have been widely explored in the detection of paracetamol in biological fluids and tablets due to their simple pretreatment procedure, high sensitivity, low time of analysis, and low costs over other analytical methods [27,28]. To understand the effect of morphology control on electrochemical performance, different morphological BiVO₄ were examined in 0.01 M PBS with and without 100 µM paracetamol using CV. All the electrochemical experiments were carried out under dark conditions in order to exclude the influence of other factors.

Figure 3A–E shows the CV response of the paracetamol re-dox process on different BiVO₄ electrodes. The CV curves of all the BiVO₄ electrodes displayed a strong anodic peak (E_pα) at 0.48 V. The different peaks at BiVO₄ electrodes could be observed in the process of backward scan with two small cathodic peaks (E_pβ), which were registered at 0.4 and 0.1 V, respectively. The chemical reaction was coupled to the electrochemical product for the oxidation of acetaminophen, i.e., N-acetyl-p-benzoquinoneimine (NAPQI) [29]. The competition between two forms of NAPQI (protonated and unprotonated species) has been proposed by Kissinger et al. [30]. The anodic peak currents in CV curves were higher than the cathodic ones, where the most probable coupled chemical reaction was the hydration of the NAPQI molecule, leading to a lower cathodic current. The limited cathodic current illustrates that the reduction of the radical intermediate is controlled by dynamics. In addition, the low cathodic current suggests that the oxidation of paracetamol on the surface of the BiVO₄ electrode is more efficient than its reduction.

Figure 3. CV curves at (A) clavate, (B) fusiform, (C) flowered, (D) bulky, and (E) particle BiVO₄ in 0.01 M PBS with and without 100 µM paracetamol. Scan rate: 100 mV s⁻¹. (F) The current densities at BiVO₄ electrode in 0.01 M PBS without (hollow icon) and with (solid icon) 100 µM paracetamol from the DPV curve. The X–axis is the peak potential at different morphologies of BiVO₄ from DPV curves.
In order to investigate the influence of morphology on the electrochemical performance, the compared CV results of BiVO$_4$ with clavate, fusiform, flowered, and bulky, as well as the reference morphology of particle shape are shown in Figure 3A–E. The reference morphology of particle BiVO$_4$ exhibited high electrochemical performance of 75 $\mu$A cm$^{-2}$ with 100 $\mu$M paracetamol when the applied potential was 0.5 V. However, the particle BiVO$_4$ showed large capacitance and a sluggish voltammetric response. The pseudocapacitance could affect the redox peak during the voltammetric response, and the extrinsic pseudocapacitance arose at the electrode surfaces along with the gradual BiVO$_4$ nanonization [31]. The bulky and flower BiVO$_4$ exhibited low current density due to their low specific surface area and poor crystallinity, respectively (Figure 3C,D). It is noted that the fusiform BiVO$_4$ with orthorhombic structure and clavate BiVO$_4$ with tetragonal structure were both covered by bismuth oxides. However, the fusiform BiVO$_4$ (Figure 3B) showed weaker catalytical performance compared with that of clavate BiVO$_4$, illustrating the tetragonal structure is beneficial for catalytic performance. Compare to BiVO$_4$ with other morphologies, the clavate BiVO$_4$ (Figure 3A) exhibited the highest electrochemical performance with a maximum redox peak current of 100 mA cm$^{-2}$ in the 0.1 M PBS solution containing 100 $\mu$M paracetamol, owing to the large specific surface area and surface oxygen vacancies, which could effectively improve the charge transfer characteristics and increase the charge diffusion coefficient of BiVO$_4$. Moreover, the clavate BiVO$_4$ could afford favorable channels for ion diffusion, which further increased the contact between the carriers and the drug molecules.

In order to suppress the influence of charging current and obtain higher sensitivity, the DPV was introduced into electrochemical analysis. The DPV experimental parameters were optimized at 50 ms pulse width, 50 mV pulse amplitude. The DPV curves of different BiVO$_4$ samples in different concentrations of paracetamol solutions are shown in Figure S5, and the electrochemical performances on morphology-dependent BiVO$_4$ electrodes in 0.01 M PBS without and with 100 $\mu$M paracetamol from DPV results are summarized in Figure 3F. Accordingly, clavate BiVO$_4$ with high crystallinity showing the highest electrochemical signal was chosen to systematically investigate its paracetamol sensing performance.

3.4. Structural Characterization of Clavate BiVO$_4$

TEM characterizations were performed on the clavate BiVO$_4$ with the length of several micrometers (Figure 4A,B). Figure 4D,E show the high magnification TEM images of clavate BiVO$_4$ that show well-resolved lattice fringes with an interlayer spacing of 0.274, 0.229, and 0.362 nm corresponding to the (112), (301), and (200) planes of tetragonal BiVO$_4$ (yellow color), respectively. Previous studies illustrated that BiVO$_4$ with high-index planes promotes the catalytic activity compared with low-index (010), (110), and (101) facets [32,33]. Thus, the clavate BiVO$_4$ with high index lanes (112), (301), and (200) at the surface could show good electrocatalytic performance. The high index lanes refer to a facet where one of the indexes is greater than 1 in (h, k, l). The lattice fringes with an interlayer spacing of 0.315 nm (white color) corresponded to the (111) crystal plane of BiO$_2$, suggesting oxidization at the surface of BiVO$_4$. The EDS data in Figure 4C depict the uniform distribution of Bi, V, and O elements. The TEM characterization proved the tetragonal structure of clavate BiVO$_4$, and the surface of BiVO$_4$ was partially covered by BiO$_2$ nanoparticles.
A linear correlation between the current density and the paracetamol concentration was obtained in the range from 5 × 10⁻⁷ to 1 × 10⁻⁵ M, which could be represented by a regression equation as follows: \( I = 4.65 \times 10^{-2} c + 5.51 \) (R² = 0.997). The detection limit of the sensor was calculated as 2 × 10⁻⁷ M (S/N = 3). The obtained DPV data revealed that the clavate BiVO₄ electrode had more competitive analytical performance and a much lower detection limit compared with BiVO₄ electrodes of other morphologies (Figure S4). The comparisons between the clavate BiVO₄ electrode and some reported electrodes for paracetamol determination are summarized in Table S1. The clavate BiVO₄ electrode exhibited analytical performances with acceptable sensitivity and a wide linear range. To evaluate the selectivity and stability of the clavate BiVO₄ electrode, metal interference ions such as K⁺, Na⁺, Ni²⁺, Zn²⁺, Co²⁺, Mg²⁺, Cd²⁺, Fe³⁺, Pd²⁺, Al³⁺, and Fe⁵⁺ were each added into a standard solution containing 100 µM paracetamol. As shown in Figure 6A, the addition of 0.10 M metal ion species did not affect the DPV current response of paracetamol on the electrode.
clavate BiVO₄ electrode. The result illustrates that the clavate BiVO₄ electrode has excellent selectivity, even in the presence of a 1000-fold concentration of interference species.

![Figure 5](image-url) (A) CV curves at the clavate BiVO₄ electrode in 100 µM paracetamol with different scan rates from 1 to 480 mV s⁻¹. Inset of (A) is a plot of the peak current against peak potential with different scan rates. Dependence of (B) logυ−logIₚ₂ and (C) Eₚ−logυ at the clavate BiVO₄ electrode. (D) DPV curves at clavate BiVO₄ electrode with the concentration of paracetamol from 0 to 100 µM. Inset of (D) shows DPV voltammograms corresponding to the high concentration of paracetamol with a 1–10 mM range.

![Figure 6](image-url) (A) Anti-interference experiment of different ions in 100 µM paracetamol with different metal ions. The concentration of the metal ions is 0.10 M. The data of current density are collected by DPV. (B) Mechanism of the electrochemical oxidation and reduction of paracetamol.

The mechanism of the electrochemical oxidation and reduction of paracetamol is shown in Figure 6B. The applied voltage promotes the separation of electrons and holes in BiVO₄. The oxidation peak of paracetamol could vary with the pH of the solution. Paracetamol converts to intermediate NAPQI easily when the pH of solution is 7.4. NAPQI
can stably exist in the solution in a deprotonated form. The CV of paracetamol shows an oxidation peak and a relatively weak reduction peak. With the progress of the reaction, NAPQI gradually transforms into benzoquinone through other intermediates. The reduction peak of benzoquinone could be observed in CV.

3.6. Determination of Paracetamol in Pharmaceutical Samples

The analytical applicability of the clavate BiVO$_4$ electrode was tested by determining the concentration of paracetamol in compound paracetamol tablets (II) (250 mg per pill). One tablet was dissolved in 0.01 M PBS solution (pH = 7.4). The concentration of paracetamol in the measured solution with a calculated concentration of 45.0 µM was detected by HPLC and DPV methods, respectively. Compared with the HPLC results, the values obtained by the DPV method exhibited high credibility. Moreover, the DPV method showed good reliability and repeatability during three times tests. The recoveries with 96.1–101.9% are given in Table 2, indicating that the fabricated clavate BiVO$_4$ sensor is accurate and sensitive enough for detecting paracetamol in pharmaceutical tablets. The above results show that the DPV method is a simple and reliable method to detect the content of paracetamol in drugs. The comparison between our work and some reported sensors for paracetamol determination were shown in Table S1. The clavate BiVO$_4$ electrode shows good stability and reliability in electrochemical detection of paracetamol.

Table 2. Analytical application of paracetamol in real samples.

| Sample            | No. | Calculated/µM | Found by HPLC/µM | Found by DPV/µM | Recovery/% |
|-------------------|-----|---------------|------------------|----------------|------------|
| Paracetamol tablets II | 1   | 45.0          | 41.4             | 42.2           | 101.9      |
|                   | 2   | 45.0          | 40.9             | 39.6           | 96.8       |
|                   | 3   | 45.0          | 40.8             | 39.2           | 96.1       |

4. Conclusions

In summary, the ability to control the morphology of BiVO$_4$ has great development prospects in high sensitivity electrochemical analysis. The BiVO$_4$ samples with different morphologies were obtained by adding different additives, and changing the pH values of the solution. The electrochemical properties of different morphology BiVO$_4$ were systematically studied in this article. The clavate BiVO$_4$ with high index lanes at the surface could solve the problem of the sluggish voltammetric response of the traditional nanoparticle on the electrode surface. The clavate BiVO$_4$ also could afford favorable channels for ion diffusion, increasing the contact between the carriers and the drug molecules. Therefore, the clavate BiVO$_4$ with a tetragonal structure exhibited the highest sensitivity and lowest detection limit among all selected BiVO$_4$ electrodes. In the DPV mode, the clavate BiVO$_4$ electrode showed linear responses over the concentration range of 0.5–100 µM ($R^2 = 0.998$) for paracetamol detection, and the LOD value was found to be 0.2 µM. The study of the relationship between morphology and electrocatalytic performance could provide very important information on the reaction activity and selectivity on target.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nano12071173/s1, Figure S1: The synthesis produces of morphology-dependent BiVO$_4$ by stirring, hydrothermal and micro wave methods. Figure S2: (A) TEM, (B) HRTEM and EDS mapping images of fusiform BiVO$_4$. TEM images of (D) flowered and (E) particle BiVO$_4$. Figure S3: High-resolution XPS spectra of V 2p, Bi 4f and O 1s. (A) clavate (B) fusiform (C) flowered, (D) bulky and (E) particle BiVO$_4$. Figure S4: DPV curves of clavate BiVO$_4$ in 0.01 M PBS with and without 100 µM paracetamol. The DPV test was performance under dark condition (labeled as dark) and in illumination condition (labeled as light). Figure S5: DPV curves at (A) fusiform (B) flowered, (C) bulky and (D) particle BiVO$_4$ in 0.01 M PBS with 0–100 µM paracetamol. Table S1: Comparison between the present work and some reported sensors for paracetamol determination. References [34–45] are cited in the supplementary materials.
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References

1. Alsultan, A.; Peloquin, C.A. Therapeutic drug monitoring in the treatment of tuberculosis: An update. Drugs 2014, 74, 839–854. [CrossRef] [PubMed]
2. Caldera, F.; Nistic, R.; Magnacca, G.; Matencio, A.; Monfared, K.; Trotta, F. Magnetic composites of dextrin-based carbonate nanosponges and iron oxide nanoparticles with potential application in targeted drug delivery. Nanomaterials 2022, 12, 754. [CrossRef] [PubMed]
3. Bateman, D.N.; Dear, J.W. Acetylcysteine in paracetamol poisoning: A perspective of 45 years of use. Br. J. Clin. Pharmacol. 2018, 84, 2218–2230. [CrossRef]
4. McCrae, J.C.; Morrison, E.E.; MacIntyre, I.M.; Dear, J.W.; Webb, D.J. Long-term adverse effects of paracetamol—a review. Br. J. Clin. Pharmacol. 2018, 84, 2218–2230. [CrossRef] [PubMed]
5. Goscianska, J.; Olejnik, A.; Ejsmont, A.; Galarda, A.; Wuttke, S. Overcoming the paracetamol dose challenge with wrinkled mesoporous carbon spheres. J. Colloid Interf. Sci. 2021, 515, 673–682. [CrossRef]
6. Wang, X.; Wu, Q.; Liu, A.; Anadón, A.; Rodriguez, J.L.; Martínez-Larrañaga, M.R.; Yuan, Z.; Martínez, M.A. Paracetamol: Overdose-induced oxidative stress toxicity, metabolism, and protective effects of various compounds In Vivo and In Vitro. Drug Metab. Rev. 2017, 49, 395–437. [CrossRef] [PubMed]
7. Boyd, E.M.; Eastham, W.N. Liver necrosis from paracetamol. Br. Med. J. 1966, 2, 497–499. [CrossRef] [PubMed]
8. Fan, Y.; Liu, J.H.; Lu, H.T.; Zhang, Q. Electrochemical behavior and voltammetric determination of paracetamol on Nafion/TiO2-graphene modified glassy carbon electrode. Colloids Surf. B 2011, 85, 289–292. [CrossRef]
9. Deroco, P.B.; Vicentini, F.C.; Fatibello-Filho, O. An electrochemical Sensor for the Simultaneous determination of paracetamol and codeine using a glassy carbon electrode modified with nickel oxide nanoparticles and carbon black. Electroanalysis 2015, 27, 2214–2220. [CrossRef]
10. Vinay, M.M.; Nayaka, Y.A. Iron oxide (Fe2O3) nanoparticles modified carbon paste electrode as an advanced material for electrochemical investigation of paracetamol and dopamine. J. Sci. Adv. Mater. Dev. 2019, 4, 442–450. [CrossRef]
11. Wu, Q.; Chen, S.; Guan, L.; Wu, H. Highly sensitive photothermal fiber sensor based on MXene device and vernier effect. Nanomaterials 2022, 12, 766. [CrossRef] [PubMed]
12. Monsef, R.; Salavati-Niasari, M. Electrochemical sensor based on a chitosan-molybdenum vanadate nanocomposite for detection of hydroxychloroquine in biological samples. J. Colloid Interface Sci. 2022, 613, 1–14. [CrossRef]
13. Zhao, P.; Ni, M.; Chen, C.; Zhou, Z.; Li, X.; Li, C.; Xie, Y.; Fei, J. Stimuli-enabled switch-like paracetamol electrochemical sensor based on thermosensitive polymer and MWCNTs-GQDs composite nanomaterial. Nanoscale 2019, 11, 7394–7403. [CrossRef] [PubMed]
14. Kim, J.H.; Lee, J.S. Elaborately modified BiVO4 photoanodes for solar water splitting. Adv. Mater. 2019, 31, 1806938. [CrossRef]
15. Baral, B.; Reddy, K.H.; Parida, K.M. Construction of M-BiVO4/T-BiVO4 isotype heterojunction for enhanced photocatalytic degradation of norfloxacin and oxygen evolution reaction. J. Colloid Interface Sci. 2019, 554, 278–295. [CrossRef] [PubMed]
16. Wang, L.; Bian, Z. Photocatalytic degradation of paracetamol on Pd-BiVO4 under visible light irradiation. Chemosphere 2020, 239, 124815. [CrossRef]
17. Orimolade, B.O.; Zwane, B.N.; Koiki, B.A.; Rivallin, M.; Bechelany, M.; Mabuba, N.; Lesage, G.; Cretin, M.; Arotiba, O.A. Coupling cathodic electro-fenton with anodic photo-electrochemical oxidation: A feasibility study on the mineralization of paracetamol. J. Environ. Chem. Eng. 2020, 8, 104394. [CrossRef]
18. da Silva Araújo, M.; Barretto, T.R.; Galvão, J.C.R.; Tarley, C.R.T.; Dall’Antònia, L.H.; de Matos, R.; Medeiros, R.A. Visible light photoelectrochemical sensor for acetaminophen determination using a glassy carbon electrode modified with BiVO4 nanoparticles. Electroanalysis 2021, 33, 663–671. [CrossRef]
19. Zaera, F. Shape-controlled nanostructures in heterogeneous catalysis. ChemSusChem 2013, 6, 1797–1820. [CrossRef]
20. Joo, J.; Kim, T.; Lee, J.; Choi, S.; Lee, K. Morphology-controlled metal sulfides and phosphides for electrochemical water splitting. Adv. Mater. 2019, 31, 1806682. [CrossRef] [PubMed]
21. Feng, J.; Li, F.; Liu, L.; Liu, X.; Qian, Y.; Ren, X.; Wang, X.; Qin, W. Ultrasensitive photoelectrochemical immunosensor for procalcitonin detection with porous nanoarray BiVO$_4$/Cu$_2$S platform as advanced signal amplification under anodic bias. *Sens. Actuators B Chem.* **2020**, *308*, 1276852. [CrossRef]

22. Santen, R.A.V. Complementary structure sensitive and insensitive catalytic relationships. *Acc. Chem. Res.* **2009**, *42*, 57–66. [CrossRef] [PubMed]

23. Tan, X.; Shen, J.; Semagina, N.; Secanell, M. Decoupling structure-sensitive deactivation mechanisms of Ir/IrO$_x$ electrocatalysts toward oxygen evolution reaction. *J. Catal.* **2019**, *371*, 57–70. [CrossRef]

24. Lu, H.; Hao, Q.; Chen, T.; Zhang, L.; Chen, D.; Ma, C.; Yao, W.; Zhu, Y. A high-performance Bi$_2$O$_3$/Bi$_2$SiO$_5$ p–n heterojunction photocatalyst induced by phase transition of Bi$_2$O$_3$. *Appl. Catal. B Environ.* **2018**, *237*, 59–67. [CrossRef]

25. Lopez, R.; Gomez, R. Band-gap energy estimation from diffuse reflectance measurements on sol–gel and commercial TiO$_2$: A comparative study. *J. Sol-Gel Sci. Technol.* **2012**, *61*, 1–7. [CrossRef]

26. Gao, Y.; Li, X.; Hu, J.; Fan, W.; Wang, F.; Xu, D.; Ding, J.; Bai, H.; Shi, W. Ag-Pi/BiVO$_4$ nanocomposite as an enhanced electrochemical sensing platform. *Sens. Actuators B Chem.* **2020**, *383*, 123962. [CrossRef]

27. Atta, N.F.; Galal, A.; Ahmed, Y.M.; El-Ads, E.H. Design strategy and preparation of a conductive layered electrochemical sensor for simultaneous determination of ascorbic acid, dobutamine, acetaminophen and amiodipine. *Sens. Actuators B Chem.* **2019**, *297*, 126648. [CrossRef]

28. Yang, L.; Zhang, B.; Xu, B.; Zhao, F.; Zeng, B. Ionic liquid functionalized 3D graphene-carbon nanotubes–AuPd nanoparticles–molecularly imprinted polymerized based paracetamol electrochemical sensor: Preparation, characterization and application. *Talanta* **2021**, *224*, 121845. [CrossRef] [PubMed]

29. Atta, N.F.; Galal, A.; Ahmed, Y.M.; El-Ads, E.H. Design strategy and preparation of a conductive layered electrochemical sensor for simultaneous determination of ascorbic acid, dobutamine, acetaminophen and amiodipine. *Sens. Actuators B Chem.* **2019**, *297*, 126648. [CrossRef]

30. Miner, D.J.; Rice, J.R.; Riggin, R.M.; Kissinger, P.T. Voltammetry of acetaminophen and its metabolites. *Anal. Chem.* **1981**, *53*, 2258–2263. [CrossRef]

31. Augustyn, V.; Simon, P.; Dunn, B. Pseudocapacitive oxide materials for high-rate electrochemical energy storage. *Energy Environ. Sci.* **2014**, *7*, 1597–1614. [CrossRef]

32. Li, P.; Chen, X.; He, H.; Zhou, X.; Zhou, Y.; Zou, Z. Polyhedral 30-faceted BiVO$_4$ microcrystals predominantly enclosed by high-index planes promoting photocatalytic water-splitting activity. *Adv. Mater.* **2018**, *30*, 170311. [CrossRef] [PubMed]

33. Liu, X.; Chen, W.; Wang, W.; Jiang, Y.; Cao, K.; Jiao, Z. F-regulate the preparation of polyhedral BiVO$_4$ enclosed by high-index facet and enhance its photocatalytic activity. *J. Colloid Interface Sci.* **2022**, *606*, 393–405. [CrossRef] [PubMed]

34. Kang, X.; Wang, J.; Wu, H.; Liu, J.; Aksay, I.A.; Lin, Y. A graphene-based electrochemical sensor for sensitive detection of paracetamol. *Talanta* **2010**, *83*, 754–759. [CrossRef]

35. Atta, N.F.; Azab, A.G.M. Electrochemical determination of paracetamol using gold nanoparticles-application in tablets and human fluids. *Int. J. Electrochem. Sci.* **2011**, *6*, 5082–5096.

36. Li, M.; Wang, W.; Chen, Z.; Song, Z.; Luo, X. Electrochemical determination of paracetamol based on Au@graphene core-shell nanoparticles doped conducting polymer PEDOT nanocomposite. *Sens. Actuat. B Chem.* **2018**, *260*, 778–785. [CrossRef]

37. Kutluay, A.; Aslanoglu, M. An electrochemical sensor prepared by sonochemical one-pot synthesis of multi-walled carbon nanotube-supported cobalt nanoparticles for the simultaneous determination of paracetamol and dopamine. *Anal. Chim. Acta* **2014**, *839*, 59–66. [CrossRef]

38. Li, J.; Liu, J.; Tan, G.; Jiang, J.; Feng, S.; Deng, M.; Qian, D.; Feng, Y.; Liu, Y. High-sensitivity paracetamol sensor based on Pd/graphene oxide nanocomposite as an enhanced electrochemical sensing platform. * Biosens. Bioelectron.* **2014**, *54*, 468–475. [CrossRef]

39. Luo, J.; Fan, C.; Wang, X.; Liu, R.; Liu, X. A novel electrochemical sensor for paracetamol based on molecularly imprinted polymeric micelles. *Sens. Actuat. B Chem.* **2018**, *260*, 909–916. [CrossRef]

40. Bonyadi, S.; Ghanbari, K.; Ghiasi, M. All-electrochemical synthesis of a three-dimensional mesoporous polymeric g-C$_3$N$_4$/PANI/CdO nanocomposite and its application as a novel sensor for the simultaneous determination of epinephrine, paracetamol, mafenefac acid, and ciprofloxacin. *New J. Chem.* **2020**, *44*, 3412. [CrossRef]

41. Wei, R. Biosynthesis of Au–Ag alloy nanoparticles for sensitive electrochemical determination of paracetamol. *Int. J. Electrochem. Sci.* **2012**, *7*, 9131–9140. [CrossRef]

42. Asadpour-Zeynali, K.; Amini, R. Nanostructured hexacyanoferrate intercalated Ni/Al layered double hydroxide modified electrode as a sensitive electrochemical sensor for paracetamol determination. *Electroanalysis* **2017**, *29*, 635–642. [CrossRef]

43. Kumar, Y.; Pramanik, P.; Das, D.K. Electrochemical detection of paracetamol and dopamine molecules using nano-particles of cobalt ferrite and manganese ferrite modified with graphite. *Heliyon* **2019**, *5*, e02031. [CrossRef]

44. Matt, S.B.; Raghavendra, S.; Shivanna, M.; Siddalingahalli, M.; Siddalingappa, D.M. Electrochemical detection of paracetamol by voltammetry techniques using pure zirconium oxide nanocomposite based modified carbon paste electrode. *J. Inorg. Organomet. Polym. Mater.* **2021**, *31*, 511–519. [CrossRef]

45. Zidan, M.; Tee, T.W.; Abdullah, A.H.; Zainal, Z.; Kheng, G.J. Electrochemical oxidation of paracetamol mediated by nanoparticles bismuth oxide modified glassy carbon Electrode. *Int. J. Electrochem. Sci.* **2011**, *6*, 279–288.