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Eco-Friendly Castor Oil-Based Delivery System with Sustained Pesticide Release and Enhanced Retention

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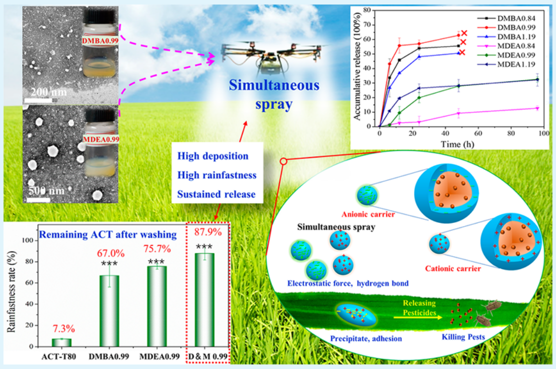

ABSTRACT: The deposition of pesticides and their retention on plant surfaces are critical challenges for modern precision agriculture, which directly affect phytosanitary treatment, bioavailability, efficacy, and the loss of pesticides. Herein, a novel and eco-friendly waterborne polyurethane delivery system was developed to enhance the spray deposition and pesticide retention on plant surfaces. More specifically, biobased cationic and anionic waterborne polyurethane dispersions were synthesized from castor oil. Both cationic and anionic polyurethane dispersions exhibited remarkable microstructural, amphiphilic, and nanoparticle morphologies with a core−shell structure that served to encapsulate a biopesticide (azadirachtin) in their hydrophobic cores (WPU-ACT). The results indicated that the cationic WPU-ACT carriers exhibited a better sustained release behavior and a better protective effect from light and heat for azadirachtin. In addition, the simultaneous spray of anionic and cationic WPU-ACT significantly enhanced the spray deposition and prolonged the retention of pesticides due to the reduced surface tension and surface precipitation induced by the electrostatic interaction when two droplets with opposite charges come into contact with each other. A field efficacy assessment also indicated that the simultaneous spray of anionic and cationic WPU-ACT could control the infestation of brown planthopper in rice crops. Castor oil-based waterborne polyurethanes in this study work as an efficient pesticide delivery system by exhibiting enhanced deposition, rainfastness, retention ability, protection, and sustained release behavior, holding great promise for spraying pesticide formulations in modern and environmentally friendly agricultural applications.

KEYWORDS: *castor oil, waterborne polyurethane, drug carriers, electrostatic force, retention, rainfastness*

■ INTRODUCTION

Pesticides are extensively used agrochemicals in modern agricultural processes for improving crop yields and maintaining a sufficient food supply. However, traditional pesticide spray formulations display certain disadvantages, such as high organic solvent contents, poor dispersibility, and low bioavailability. During the spraying process, more than 50% of these pesticides are lost because of poor retention characteristics on hydrophobic plant surfaces.[1] Accounting for evaporation, spraying drift, and runoff from the plant surfaces, traditional pesticide formulations are not efficiently utilized (the effective utilization rate is typically less than 10%).[2] Owing to photolysis, decomposition, and rain washing, only 0.1% of pesticides are able to reach their targets (Figure S1).[3,4] Therefore, pesticides are frequently used in excessive amounts for effectively controlling pests or weeds. Most of the liquid from the agricultural sprays are washed out to the soil and groundwater and thus pollute the environment and endanger human health.[5,6]

To overcome these drawbacks of conventional pesticide formulations and extend their duration of action on crops while reducing production costs, the behavior and impact of spraying plant surfaces have been extensively studied.[7] Retention and deposition of the sprayed pesticide critically depend upon the chemical formulation, climatic conditions, and spray techniques.[8] However, the size, surface tension, and viscosity of the formulation directly affect its retention and rainfastness. The addition of surfactants into water drops can reduce the surface tension,[6,9−11] while adding flexible polymers can provide a dissipative force for the pesticide formulation;[12,13] these additions thereby prolong their retention on plant surfaces. However, a high speed impinging water droplet typically bounces off superhydrophobic surfaces during spraying process, which suppresses the antirebound effect of

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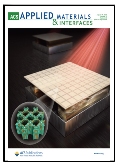

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Table 1. Theoretical Composition, Z-Average Size, ζ Potential, Drug Loading Capacity (LC), and Encapsulation Efficiency of WPU-ACT Emulsions

samples	molar ratio NCO (IPDI):OH (CO):OH (chain extender)	Z-average size (nm)	ζ potential (mV)	storage life (month)	LC (wt %)	EE (%)	pH
DMBA0.69	1.70:1.00:0.69	116.10 ± 17.32	−42.6 ± 3.0	>12	9.37 ± 0.27	94.00 ± 0.71	7.31 ± 0.02
DMBA0.84	1.85:1.00:0.84	78.56 ± 0.42	−40.1 ± 3.1	>12	9.41 ± 0.09	93.64 ± 0.73	7.20 ± 0.01
DMBA0.99	2.00:1.00:0.99	48.52 ± 0.37	−39.6 ± 3.2	>12	9.40 ± 0.21	95.43 ± 1.37	7.29 ± 0.01
DMBA1.19	2.20:1.00:1.19	30.15 ± 0.59	−45.5 ± 2.6	>12	9.49 ± 0.15	95.28 ± 1.09	7.10 ± 0.03
MDEA0.69	1.70:1.00:0.69	642.80 ± 15.70	77.8 ± 6.1	<1			4.10 ± 0.03
MDEA0.84	1.85:1.00:0.84	143.20 ± 9.92	51.6 ± 3.0	>12	9.58 ± 0.14	94.67 ± 0.95	4.90 ± 0.04
MDEA0.99	2.00:1.00:0.99	81.77 ± 2.95	52.9 ± 4.2	>12	9.23 ± 0.33	94.13 ± 1.31	4.30 ± 0.01
MDEA1.19	2.20:1.00:1.19	54.27 ± 0.62	59.5 ± 4.7	>12	9.41 ± 0.29	93.91 ± 1.99	4.36 ± 0.05

surfactants.[14,15] In addition, surfactants create smaller droplets in the spray, aggravating wind drift and evaporation.[16]

Therefore, Maher Damak[6] proposed an alternative approach to enhance drop deposition rate: the addition of small amounts of oppositely charged polyelectrolytes to the sprays, which can alter the surface properties of the target *in situ* by forming sparse hydrophilic defects on the substrate. When two droplets containing oppositely charged polyelectrolytes collide, macromolecules with opposite charges are attracted to each other and to other molecules and finally form precipitates, which highly extends the retention of the droplets on superhydrophobic surfaces. However, this technique directly complicates conventional pesticide formulations and adds a new unknown interaction between polyelectrolytes and pesticides, which could affect their stability and efficacy. What is more, these pesticide formulations with antirebound modifications are still susceptible to rain washing.

Alternatively, advanced pesticide delivery systems based on inorganic and polymer materials could improve leaf adhesion, providing a sustained effect by maintaining the controlled release rate and thus protecting the activity of pesticides over a specified period of time.[17,18] Recently, various novel, degradable, and sustainable polymer carriers have been developed to address plastic pollution and the dependence on fossil feedstock.[19−21] Polyurethanes with excellent molecular tailoring abilities, mechanical properties, biocompatibilities, and controllable degradation properties[22−24] have been extensively applied in coatings, adhesives, sealants, foams, and biomedical devices, especially as drug carriers for hydrophobic drugs[25] and high toxic antitumor drugs[24,26−30] to solve issues with insolubility, instability, excessive therapeutic doses, and side effects of drugs by controlling the drug release and targeting ability. Polyurethane-based pesticide delivery systems have also been developed to encapsulate highly toxic water-soluble[31] or hydrophobic[32] pesticides to improve the stability of active ingredients in agriculture. Taking environmental and ecological factors into consideration, eco-friendly waterborne polyurethanes, especially those prepared from vegetable oils,[33−36] that use water as a dispersion medium instead of organic solvents are promising candidates for pesticide delivery systems. Chengyou Kan[37] encapsulated avermectin with waterborne polyurethane carriers through an emulsion solvent evaporation method for achieving controlled release and enhancing efficiency of the pesticides. They also demonstrated that the drug delivery system could enhance foliage adhesion through hydrogen bonding between polyurethane latex films and hydroxyl, carboxyl, or aldehyde groups on the foliage surface after the volatilization of water.[19] Unfortunately, the antirebound behavior of these pesticide carrier droplets is still unclear.

Therefore, the development of pesticide formulations that provide a good antirebound effect, a controlled release, and rainfastness that thus extends their duration of action on crops, reduces their waste, and protects the environment is a huge challenge in the agricultural field. Thus, a novel oppositely charged drug delivery system has been prepared from waterborne polyurethanes (WPU) using an eco-friendly castor oil derivative (CO208; OH number, 208 mg of KOH per gram), 2,2-bis(hydroxymethyl)butyric acid (DMBA), and *N*-methyl diethanolamine (MDEA) (as chain extenders). Azadirachtin (ACT), a biodegradable and optically unstable pesticide,[17] was adopted in this delivery system, and the pesticide protective property of the WPU carrier was studied. The drug loading capacity, release behaviors, spray deposition, rainfastness, and field efficiency of the carrier and the stability of ACT in WPU emulsions and films were systematically investigated. In particular, anionic and cationic waterborne polyurethane ACT-loaded (WPU-ACT) emulsions were simultaneously sprayed and compared with a single spray to verify the enormous advantage of the oppositely charged delivery system benefiting from electrostatic interactions.

The pesticide delivery system described herein combines advantageous features of previously reported systems, including an improved antirebound effect, a sustained release, and rainfastness properties, into a single formulation. The approach investigated makes use of cationic and anionic bio-based polyurethane core−shell structures to encapsulate a pesticide. The simultaneous spraying of cationic and anionic polyurethane dispersions results in a better retention of the pesticide onto the plant surface along with the limited rebounding of formulation droplets. The combination of these properties into a single bio-based system has not been previously achieved.

■ EXPERIMENTAL SECTION

Materials and Methods. Unless mentioned otherwise, all chemical reagents were obtained from commercial suppliers and used without any additional purification. Castor oil (CO164; OH number, 164 mg of KOH per gram) was procured from Fuyu Chemical Company. The castor oil derivative (CO208; OH number, 208 mg of KOH per gram) was purchased from Guangzhou Xinye Trading Company. Isophorone diisocyanate (IPDI), triethylamine, and acetic acid were procured from Aladdin Reagent. Dimethylol butanoic acid (DMBA), dimethylol propionic acid (DMPA), and *N*-methyl diethanolamine (MDEA) were purchased from Adamas. Dibutyltin dilaurate (DBTDL) was procured from the Fuchen Chemical Reagent Factory. Methyl ethyl ketone (MEK) was purchased from Tianjin Hongda Chemical reagent. ACT was extracted by the Key Laboratory of Natural Pesticides and Chemical Biology, Education Ministry, South China Agricultural University

(ACT available content 39.45%). Unless mentioned otherwise, ACT represents the crude extracts in this manuscript.

Synthesis of WPU Emulsions Without Loading ACT. Castor oil-based cationic and anionic WPUs were synthesized; the feed ratios are listed in Table S1. First, IPDI, castor oil (5g), and the chain extender were mixed thoroughly with continuous mechanical stirring for 10 min at 78 °C. Then, 10 μL of DBTDL was added until the mixture lost its flowability, and 18−20 mL of MEK was added to reduce the viscosity. The mixture was allowed to react under continuous stirring for 2 h at 78 °C and was then cooled to room temperature. Neutralizer TEA (for DMBA and DMPA) or acetic acid (for MDEA) was added with continuous stirring. Finally, a certain amount of deionized water was slowly added into the system, with a high stirring speed of 600 rpm for 2h. MEK was completely removed through vacuum rotary evaporation, and the WPU emulsions were obtained with a 15 wt % solid content. These WPU emulsions were denoted as *X*DMBA*n*, *X*DMPA*n*, and *X*MDEA*n* ($X = 164$, $n = 0.69$, 0.84, 0.99, or 1.19), where *X* represented the OH number of the castor oil used and *n* represented the molar ratio of the ionic functional groups (Table S1).

Synthesis of WPU-ACT Emulsions. Castor oil-based cationic and anionic WPU-ACTs were synthesized according to the feed ratios listed in Table 1. First, IPDI, castor oil 208 (5g), and the chain extender (DMBA or MDEA) were mixed thoroughly with mechanical stirring for 10 min at 78 °C. Then, 10 μL of DBTDL was added until the mixture lost its flowability, and 18−20 mL of MEK was added to reduce the viscosity. The mixture was allowed to react under continuous stirring for 2 h at 78 °C, and was then cooled to room temperature. TEA (for DMBA) or acetic acid (for MDEA) was added with continuous stirring. ACT was then added, and stirring continued for 30 min in the dark (10% dosing ratio). Finally, deionized water was slowly added into the system, with a high stirring speed of 600 rpm for 2h. MEK was completely removed through vacuum rotary evaporation, and the oppositely charged WPU-ACT emulsions were obtained with a 15 wt % content, where the solid content of ACT was 1.5 wt %. These WPU-ACT emulsions were denoted as DMBA*n* and MDEA*n* ($n = 0.69$, 0.84, 0.99, or 1.19), where *n* represented the molar ratio of the ionic functional groups (Table 1). An ACT aqueous suspension in 0.2% Tween-80 (ACT-T80) was prepared as a comparison (the solid content of ACT was 1.5 wt %, which was the same as that in the WPU-ACT drug-loaded system). The ACT concentrations of the WPU-ACT emulsions and ACT-T80 were determined through high-performance liquid chromatography (HPLC) and denoted as C_0.

After storage at 4, 40, and 54 °C for 7 days and 28 days, respectively, the particle size and ζ potential of these WPU-ACT emulsions were measured to determine their storage stability.

Drug Loading. The WPU-ACT emulsions were passed through a syringe filter with a 0.45 μm pore size (Millipore, Carrigtwohill Co., Cork, Ireland) to remove any unloaded insoluble ACT. A measured amount of a filtered WPU-ACT emulsion was added to the empty vial and freeze dried. Then, a certain amount of the WPU-ACT solid sample (M) and 10 mL of acetonitrile were charged into a 50 mL centrifuge tube, and the tube was placed in an ultrasonic bath for 30−60 min to completely dissolve the loaded ACT. Then, the mixture was centrifuged at 3000 r/min for 15 min, the supernatant was collected, and the loaded ACT amount (m) in the supernatant was determined by HPLC. The drug loading content (LC, %) and the encapsulation efficiency (EE, %) were calculated using the following equations:[38]

$$\mathrm{LC} = m/M \times 100\%$$

$$\mathrm{EE} = m/m_0 \times 100\%$$

where m is the mass of the loaded ACT in the WPU-ACT solid powder, M is the mass of WPU-ACT solid powder, and m_0 is the mass of ACT that was actually added to the WPU-ACT solid preparation.

Environmental Stability of the WPU-ACT Drug-Loaded System. The ACT concentrations of the WPU-ACT emulsions and ACT-T80 were determined through HPLC and are denoted as C_0.

For thermal stability measurements, WPU-ACT emulsions (15 wt %) and ACT-T80 were kept in a dark environment at 40 and 54 °C for 7 d. Then, 100 μL of the WPU-ACT emulsions and ACT-T80 were withdrawn and diluted 100× with acetonitrile. The residual ACT concentration (C_m) was measured using HPLC. The decomposition rate of ACT was calculated as $(C_0 - C_m)/C_0 \times 100\%$

For photostability measurements, 200 μL of the WPU-ACT emulsions were placed in glass vials and dried at room temperature for 3 days in dark conditions to prepare the test samples. ACT-T80 was also added to the glass vials and kept at similar conditions as a blank control. Then, all samples were exposed to the outdoor sunlight (at Guangzhou, Guangdong, China). The exposed samples were collected after 3 days and 7 days, and the amount of residual ACT (C_t) was measured using HPLC, as mentioned above. The decomposition rate was calculated as $(C_0 - C_t)/C_0 \times 100\%$

Release Behavior of WPU-ACT Emulsions. WPU-ACT emulsions (2 mL) were added into dialysis bags (cutting MW = 3500 Da), and the bags were then immersed into 100 mL of the release medium (0.2% Tween-80 solution in distilled water) in 250 mL brown jars at 30 °C. Surfactant Tween-80 was added to the release medium to better disperse the hydrophobic ACT.[39] At predetermined time intervals, 3 mL of the release medium was withdrawn from the jar, and 3 mL of fresh Tween-80 solution was replenished into the jar. Then, the sampled release medium was filtered through a syringe filter with a 0.22 μm pore size. The release studies were conducted in triplicate. The cumulative release profiles of ACT were determined using HPLC.

Release Behavior of WPU-ACT Films. WPU-ACT emulsions (200 μL) were added to brown glass vials and dried at room temperature for 3 days in dark conditions, and the ACT contents of the WPU-ACT films were measured. Then, 2 mL of the 0.2% Tween-80 release medium was added at 30 °C. At predetermined time intervals, the entire amount of release medium was withdrawn from the jar, and 2 mL of fresh Tween-80 solution was replenished into the jar. Then, the sampled release medium was passed through a syringe filter with a 0.22 μm pore size. The release studies were performed in triplicate. The cumulative release profiles of ACT were determined using HPLC.

Deposition Property of the WPU-ACT Emulsions. The WPU-ACT emulsions were diluted to 1 wt % (the theoretical content of ACT was 0.1 wt %) in deionized water before the study to prepare the spraying formulations. The control sample was prepared in a similar manner by diluting ACT-T80 in deionized water (the theoretical content of ACT was 0.1 wt %). Glass slides were siliconized to simulate the plant leaf.[40] The test slides were immobilized at a slope of 45°, while the horizontally mounted slides were used to record the spray deposition per unit ground area.[41] Then, identical volumes (V_s) of all the ACT formulations were sprayed ton the siliconized glass slides. Anionic WPU-ACT (0.5 V_s) and cationic WPU-ACT (0.5 V_s) were simultaneously sprayed and recorded as D&M*n* ($n = 0.84$, 0.99, or 1.19). Water was used as the blank control. The additional weight of the slides with the 45° incline was recorded as W_t, while the additional weight of the horizontal siliconized glass slides was recorded as W_0. Each test was performed in ten replicates. The retention ratio (R_r, %) was calculated according to the equation $R_r = W_t/(W_0) \times 100\%$.

Laboratory-Scale Wash Off. According to a previous study,[42] ACT spraying formulations (ACT-T80, DMBA0.99, MDEA0.99, and D&M0.99) containing same amount of ACT (a theoretical content of 0.1%) were sprayed on the rice leaf surface and allowed to dry for 2 h. The leaves were fixed to a filter paper at an angle of 45° and then washed with deionized water at a flow rate of 3 mL/min from a height of 20 cm for 30 min (to simulate natural rain). Coated leaves (1 × 1 cm^2) before and after washing were immersed in acetonitrile, and the mixutre was ultrasonicated for 30 min. Then, the filtrates were analyzed by HPLC. The ACT concentrations on rice leaves before and after washing were denoted as C_b and C_a. Each test was conducted in five replicates. The rainfastness (R_f, %) was calculated based on the equation $R_f = C_a/(C_b) \times 100\%$. The surface morphology

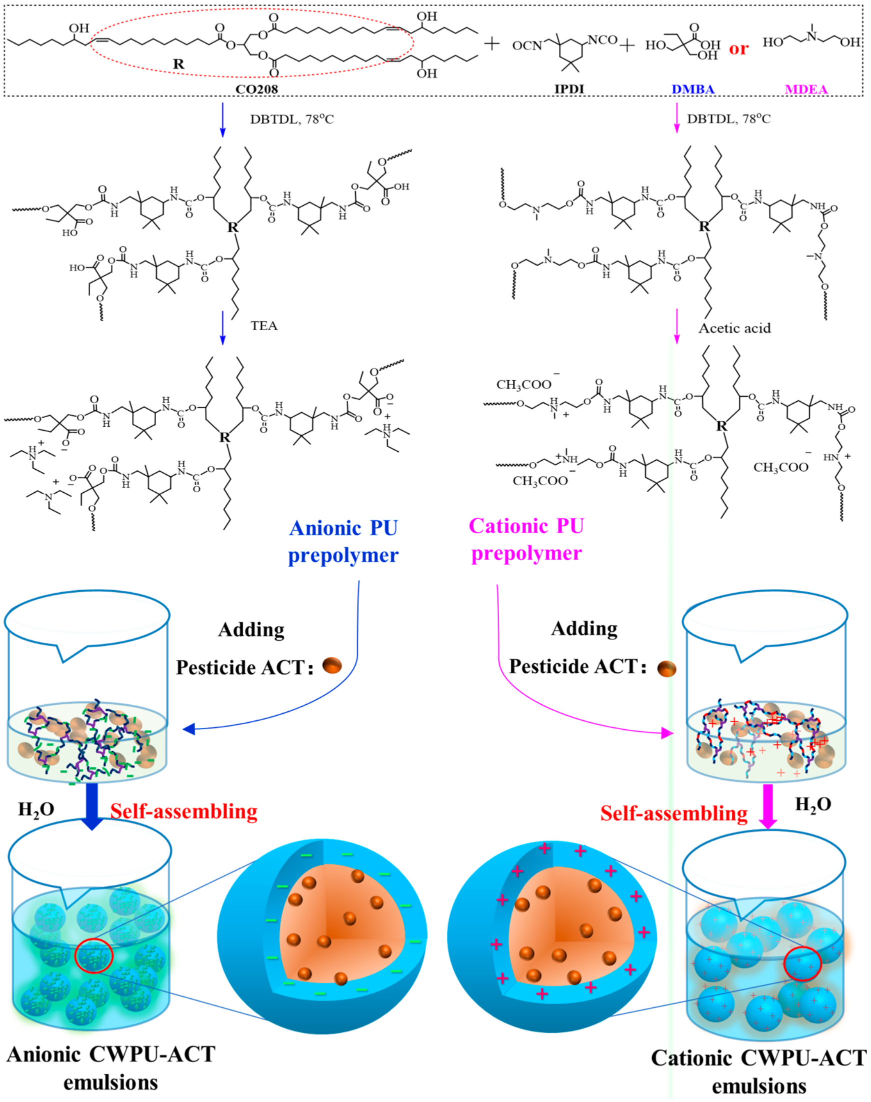

Figure 1. Schematic of the synthesis of WPU-ACT emulsions.

of the rice leaves before and after washing was observed under a scanning electron microscope.

Field Efficacy Assessment. Field experiments were conducted against a brown planthopper following Chinese Pesticide Guidelines for Field Efficacy Trials (II) (GB/T17980.4-2000) at Huadu District, Guangzhou, Guangdong, China, from June to July 2019. The field for the experiment was divided into five treatment areas (approximately 15 m^2 for each area, which was randomly assigned in the experimental field), and a ridge 10−15 cm long was built to prevent the flow of water to the adjacent treatment areas. All the ACT formulations were diluted by water (the concentration of ACT was 15 μg/mL) and sprayed with a concentration of 0.3 mg/m^2 of ACT. Areas 1−5 were treated with water, ACT-T 80, DMBA0.99, MDEA0.99, and D&M0.99, respectively, while water treatment area 1 was the blank control. Each treatment was performed in five replicates. The numbers of brown planthoppers were counted before and after spraying the ACT formulations for 1, 3, 5, and 10 days according to the cater-corner mode per subdistrict.

The control effect of these ACT formulations was calculated as

$$\text{Control effect (\%)} = \left(1 - \frac{\text{CK}_0 \times \text{PT}_1}{\text{CK}_1 \times \text{PT}_0}\right) \times 100\%$$

where PT_0 represents the pest number before the treatment in the test area, PT_1 is the pest number after the treatment in the test area, CK_0 is the pest number before the treatment in the blank control area, and CK_1 is the pest number after the treatment in the blank control area.

Characterization. The surface tension of the WPU-ACT emulsions was determined using a drop shape analysis system DSA 100 (Krüss, Hamburg, Germany) by following the pendant-drop method at room temperature. The results were calculated as the mean value for three replicates. The contact angles of the droplets of ACT solution (3 μL droplets, 0.1% ACT) on the hydrophobic siliconized glass slides were measured following the sessile drop method. The stability of the WPU-ACT emulsions was evaluated by centrifuging the emulsions at 3000 rpm for 60 min using a Tomos 3-18 centrifuge. The particle size and ζ potential of the WPU-ACT emulsions (diluted with distilled water to about 0.01 wt % before the test) were measured using a Zetasizer Nano ZS dynamic light-scattering (DLS) instrument (Malvern, UK) at 25 °C at an angle of 90°. The microscopic structure of the WPU-ACT emulsions was observed under a transmission electron microscope (Tecnai 12, FEI Company, Netherlands). A drop of the WPU-ACT emulsion (0.1 wt %) was placed on a copper grid, and the excess fluid was blotted off. Then, the copper grid was stained with 1% (w/v) phosphotungstic acid and air-dried before measurement.

HPLC was performed using an Agilent 1260 spectrometer at room temperature with Agilent XDB-C18 chromatographic column (250 mm × 4.6 mm × 5 μm) and a UV−vis detector at 215 nm. The flow rate was 1.0 mL/min, and the mobile phase consisted of acetonitrile/

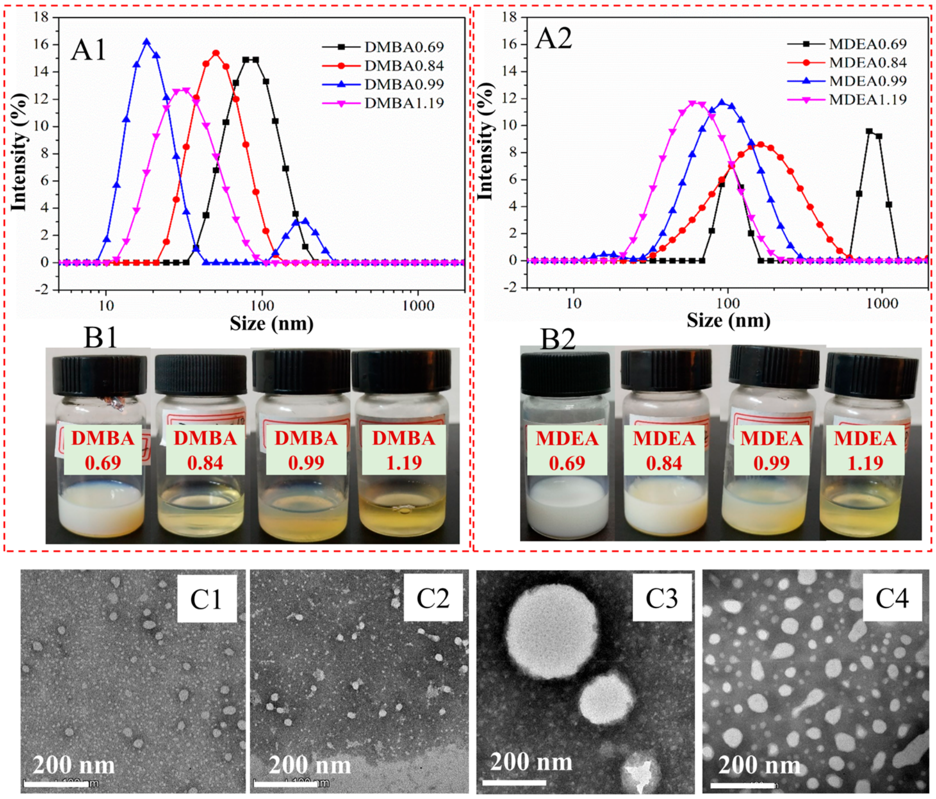

Figure 2. Particle size distribution and appearance, respectively, of WPU-ACT emulsions with different chain extenders (A1 and B1) DMBA and (A2 and B2) MDEA and TEM images of WPU-ACT emulsions (C1) DMBA0.84, (C2) DMBA0.99, (C3) MDEA0.84, and (C4) MDEA0.99.

water (40:60 v/v). Under these test conditions, the retention time of the ACT was 12.20 min. Under the same integral conditions, the area under the curve was calculated, and the content of ACT was assessed. These results were reported as the mean value for three replicates. To plot the calibration curve, different concentrations of the ACT solution (0.01−1.00 mg/mL) were prepared in acetonitrile and then injected into the HPLC system.

A pH meter (SevenCompact, S210, Mettler Toledo) was used to measure pH values of the WPU-ACT emulsions. Scanning electron microscopic (SEM) images were captured using an SEM instrument (Inspect F, FEI Company) at an accelerated voltage of 5 kV. After the laboratory-scale wash off experiment, a small piece of rice leaf was cut and lyophilized before and after washing. All samples were gold sputtered prior to imaging.

Statistical Analysis. The Statistical Package for the Social Sciences (SPSS, ver. 19.0) software was used for statistical comparisons through a one-way analysis of variance (ANOVA). Data were expressed as the mean ± standard deviation (SD). The statistical significance was $^*p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.005$.

RESULTS AND DISCUSSION

Properties of WPU-ACT Emulsions. Waterborne polyurethane dispersions without ACT were successfully prepared from CO164 and CO208 with DMPA, DMBA, and MDEA (as chain extenders). The particle size and surface tension of these dispersions were measured (Table S1 and Figure S2). The particle sizes measured by DLS ranged from 29.86 to 196.30 nm, making them good candidates for the nanodrug delivery system. The surface tensions of WPUs from castor oil 208 (57.53 to 64.06 mN/m) were lower than those from CO164 (67.51 to 71.17 mN/m) with the same solid concentration (1 g/L) because an increase in the OH number of the castor oil enhanced the number of hydrophilic ionic groups (carboxylate and quaternary ammonium salt) of the polyurethanes, therefore reducing the surface tension (the surface tension of water at 20 °C is 72.75 mN/m). A low surface tension would favor the retention of droplets on the plant surface; therefore, WPUs from CO208 were selected as the pesticides' carriers. Biodegradable commercialized hydrophobic ACT was selected as the model drug, which was self-assembled in the hydrophobic core of the polyurethane particles as shown in Figure 1.

Drug loading capacity (LC) and encapsulation efficiency (EE) are critical parameters in drug delivery systems. As indicated in Table 1, the measured EE was more than 90% and the LC ranged from 9.0% to 9.5%, demonstrating that most of the ACT was loaded in the WPU carrier. The loaded carriers (WPU-ACT) exhibited a unimodal size distribution, and the particle sizes determined by DLS ranged from 30.15 to 642.80 nm (Table1 and Figure 2A1 and A2), which were larger than those of the corresponding WPU emulsions without ACT (Table S1) because of the volume occupied by the hydrophobic ACT after encapsulation in the particle core.[4] In addition, TEM images indicate that ACT-loaded carriers possess a spherical morphology with no appreciable change to the micelle size obtained by DLS (Figure 2), as well as the higher chain extender content in the corresponding polyurethanes, the more transparent of which are the resulting WPU-ACT emulsions, and the smaller particle size of these emulsions because of the higher content of hydrophilic groups (Figure 2B1 and B2). Cationic WPU-ACT emulsions exhibit larger particles compared to anionic WPU-ACT emulsions, which can be explained by the structures of ACT and the polyurethanes. ACT, possessing ester and hydroxy groups, can easily form hydrogen bonds.[43] Anionic waterborne polyurethane with DMBA can provide more hydrogen bonding sites

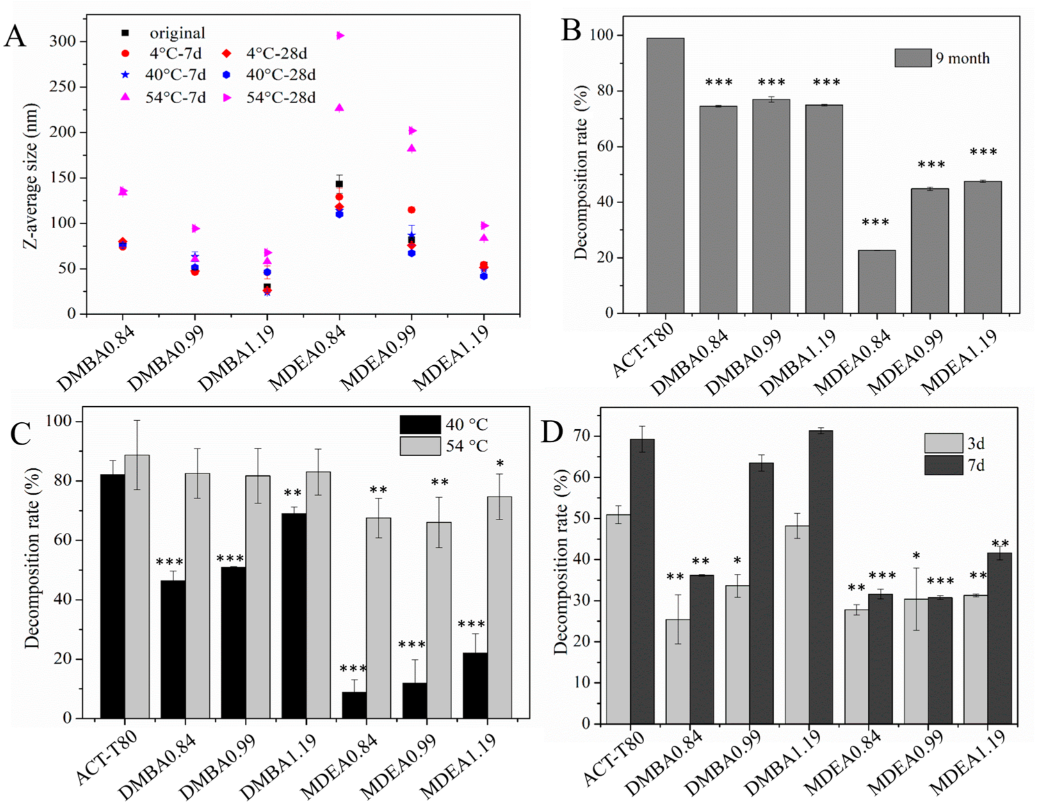

Figure 3. Stability of WPU-ACT emulsions. (A) The Z-average size of WPU-ACT emulsions after storage at 4, 40, and 54 °C for 7−28 days. (B) The ACT amount of residue after storage at 4 °C for 260 days. (C) The decomposition rate of ACT in WPU-ACT emulsions after storage at 40 and 54 °C for 7 days. (D) The decomposition rate of ACT in WPU-ACT films under sunlight. The statistical significance is $*p < 0.05$, $**p < 0.01$, and $***p < 0.005$.

than cationic waterborne polyurethane MDEA.[44,45] Therefore, ACT has a stronger interaction with anionic WPU nanoparticles than with cationic WPU nanoparticles, leading to smaller particles.

Due to the incorporation of a carboxyl (in DMBA) and a tertiary amine (MDEA) into the hydrophilic shell, the corresponding emulsions displayed negative surface charges ranging from −39.6 to −45.5 mV, as well as positive surface charges of 51.6−77.8 mV after neutralization (Table 1). WPU-ACT emulsions exhibited an excellent stability, and no precipitation or stratification occurred when these WPU-ACT samples were centrifuged at 3000 rpm for 60 min (except for MDEA0.69) (Table 1). Therefore, all the following tests were conducted without DMBA0.69 and MDEA0.69.

After storage at 4 and 40 °C for 7−28 days, the hydrodynamic diameter and ζ potential of these CWPU-ACT emulsions displayed few changes with time (Figure 3A and Table S2). When the storage temperature was increased to 54 °C, some particles aggregated, leading to an increase in the particle size (Figure 3A). Overall, no precipitates were observed at the different storage temperatures evaluated. Furthermore, the absolute ζ potential values of samples stored at different temperatures were higher than 30 mV, indicating the excellent physical stability of these WPU-ACT emulsions.[46,47]

ACT is a good alternative to conventional insecticides, displaying no resistance problems due to its chemical complexity and nontoxic nature to mammals, beneficial arthropods, and warm-blooded vertebrates.[48] Unfortunately, ACT has a rapid biodegradability, especially in regard to photothermal factors that would accelerate its decomposition,[17,49,50] which greatly limits its application ranges in the agricultural field. Our results indicated that the decomposition rate of ACT after encapsulation in the WPU carrier was much slower than that of free ACT. After storage at 4 °C for 260 days in dark conditions, ACT in ACT-T80 was almost completely decomposed, while the decomposition rate of ACT in MDEA0.84 was only 22.7% (Figure 3B). Similarly, after storage at 40 °C for 7 days, cationic WPU-ACT emulsions exhibited the highest protective effect than anionic WPU-ACT emulsions and ACT-T80 (Figure 3C). Additionally, the higher chain extender content in the corresponding polyurethanes was, the the higher the degradation of ACT in the WPU-ACT emulsions. After storage at 54 °C for 7 days, ACT from all WPU-ACT emulsions and ACT-T80 were degraded, indicating the poor stability of ACT at high temperatures compared with that at 40 °C. However, it was still observed that ACT from cationic WPU-ACT emulsions decomposed slower in these samples (Figure 3C). These phenomena might be attributed to the pH of the WPU-ACT emulsions (Table 1). ACT is mostly stable in mild acidic aqueous solutions between pH 4−6, while it is unstable in mild alkaline and strong acidic solutions where it is rapidly degraded or altered by heat.[51] The decomposition test was performed for the original emulsions without additional media. There was no obvious concentration and osmotic pressure differences between the pesticide-loaded particle and the media. The pesticide release and self-assembly of the pesticide loading[19,37] would achieve equilibrium. The released free ACT was much more stable in the acidic environment of cationic WPU-ACT emulsions than in the

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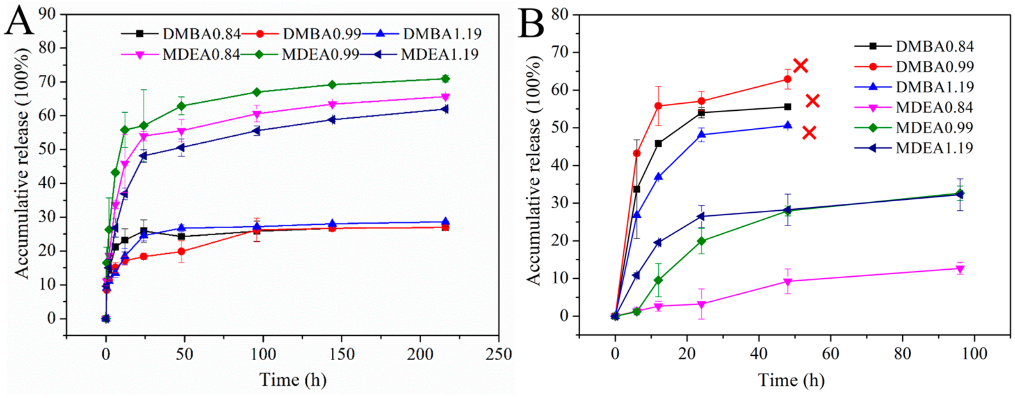

Figure 4. Drug release profile of WPU-ACT (A) emulsions and (B) films. The red forks indicate that the corresponding films swelled and fractured after 48 h.

alkaline environment of anionic WPU-ACT emulsions. The cationic WPU carrier with pH values ranging from 4.30 to 4.90 displayed a better protective effect for ACT than the anionic WPU carriers with pH values ranging from 7.10 to 7.29.

The photostability of ACT was also determined after exposure under sunlight. ACT-T80 was used as the control. The results are plotted in Figure 3D. Apparently, the decomposition rate of ACT in the WPU-ACT drug-loaded system was slower than that of free ACT because of the UV-shielding and protective effect of the WPU carrier. Furthermore, ACT slowly degraded in the cationic WPU-ACT drug-loaded system compared with the anionic drug-loaded system because of the acid−base environment of the initial WPU emulsions. Thus, the cationic WPU-ACT drug-loaded system with a better thermostability and photostability aid in decelerating the degradation of ACT in an agricultural application, while the anionic WPU can be used as a carrier of other pesticides, which would synergize with ACT in a future study.

Release Behavior of the WPU-ACT Emulsions and Solid Films. The release behavior of the WPU-ACT emulsions is shown in Figure 4A. The release data of ACT in the WPU-ACT emulsions were mainly fitted to the first-order kinetic model (R^2 values ranging from 0.822 to 0.946) and the Korsmeyer−Peppas model (R^2 values ranging from 0.915 to 0.985), as illustrated in Figure S3 and Table S3. The first-order model describes the adsorption and removal of substances in media, while Korsmeyer−Peppas model can describe the release of a substance from a polymeric system. Parameter "n" in the release kinetic models could be used to characterize the release mechanisms, where $n \leq 0.50$ (Fickian diffusion), $0.50 < n < 1$ (anomalous transport), and $n = 1$ (case II transport, i.e., zero-order release).[52] The value of the "n" parameter for all WPU-ACT emulsions ranged from 0.124 to 0.240, representing a Fickian diffusion release mechanism where the concentration and osmotic pressure difference strongly affect the pesticide release.

All the WPU-ACT carriers showed a relatively high release rate initially and a slower release afterward in a 0.2% Tween-80 aqueous solution. Two reasons were responsible for the initial fast release of ACT: (1) the nonuniform distribution of ACT in the WPU nanoparticles, where some free ACT molecules and those ACT molecules attached to the surface of the particle would be released more quickly than the ACT molecules from the core of the nanoparticles,[37] and (2) the difference in the internal and external concentrations that induced the osmotic pressure and accelerated the diffusion process at the higher initial concentration of ACT. In addition, cationic WPU-ACT emulsions exhibited a higher release rate than anionic WPU-ACT. The possible reason for this was that ACT had stronger hydrogen bonding with anionic WPU nanoparticles than with cationic WPU nanoparticles,[44,45] which made the release of ACT from anionic WPU-ACT nanoparticles harder.

In practical applications, WPU-ACT emulsions were sprayed and then formed films on the crops. It is necessary to study the release behavior of ACT from WPU-ACT films. The release data of ACT in WPU-ACT emulsions were mainly fitted to the first-order kinetic model (R^2 values ranging from 0.940 to 0.998) and the Korsmeyer−Peppas model (R^2 values ranging from 0.897 to 0.985), as illustrated in Figure S3 and Table S4. WPU-ACT films also show a Fickian diffusion release mechanism in the 0.2 wt % Tween-80 aqueous solution. The stability and swelling properties of these films significantly influenced the release behavior. In the film release test, anionic WPU-ACT films started to fracture after 24 h and then form tiny fragments after 48 h, while cationic WPU-ACT films were uniform and complete during the entire release time. Therefore, the release rate of the cationic WPU-ACT drug release system was much slower than that of the anionic WPU-ACT films (Figure 4B).

Deposition Property and Rainfastness of WPU-ACT Emulsions. Laboratory scale spraying experiments were conducted on siliconized glass slides and rice leaves to investigate the deposition of pesticides, and the results are illustrated in Figure 5. The deposition rate of single ACT formulations ranged from 55.2% to 68.8%, which was much higher than that of the water spray (42.9%) because the polymer and surfactant (Tween-80) could reduce the surface tension of droplets. Indeed, the surface tension of the ACT formulations ranged from 53.12 to 54.85 mN/m, while the surface tension of a water droplet at 20 °C corresponds to 72.75 mN/m. The decrease in the surface tension improved the spreading of pesticides on hydrophobic surfaces (Table S5).To eliminate the pH influence of these samples on the deposition property, ACT in a Tween 80 aqueous solutions at pH 4.5, 5.6, and 7.2 were prepared. The deposition results are recorded in Table S6 and indicate that there is no significant difference in the deposition property at different pH values. When anionic and cationic WPU-ACT emulsions were simultaneously sprayed, the deposition rate was much higher than a single spray, which could reach up to 89.2%

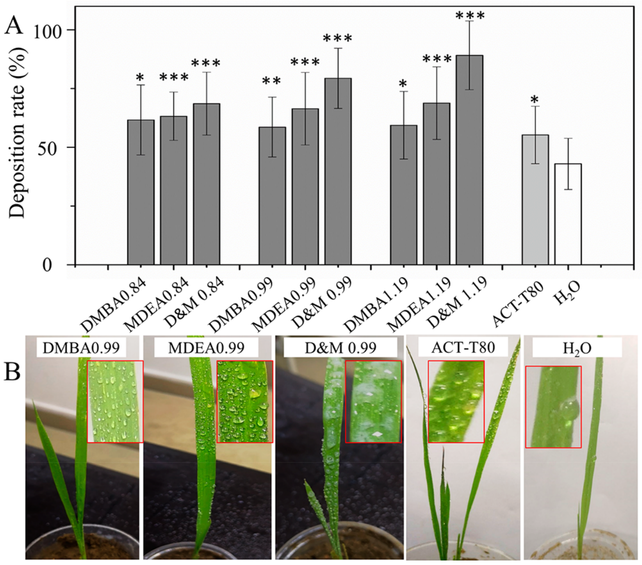

Figure 5. Deposition of different ACT formulations with a certain concentration of ACT (theoretical content of 0.1 wt %). (A) The deposition ratio of these dilute WPU-ACT emulsions on siliconized glass slides. (B) Spraying dilute WPU-ACT emulsions on rice. The statistical significance is $^{*}p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.005$.

(D&M1.19). Two reasons were responsible for the highest deposition rate for the simultaneous spray. The first reason relates to the reduced surface tension, as discussed above. The second reason is associated with the easy formation of precipitates or gels from droplets that stick to the leaf surface (Figure 5B, D&M0.99). Droplets with oppositely charged particles in close proximity were attracted to each other by electrostatic forces and subsequently attracted other particles to form precipitates.[6] The precipitates exhibited a high adhesion to the leaf surface and increased their retention on the plant surface.

To better understand the electrostatic interaction between anionic and cationic WPU-ACT emulsions, a series of WPU-ACT blends with different anionic and cationic ratios (DMBA*n*:MDEA*n* = 1:5, 2:4, 3:3, 4:2, and 5:1) were prepared. Precipitates were formed in the mixing process when the solid content of the WPU-ACT emulsions was consistent with that of the spraying formulations (1 wt %) (Figure 6A). Thus, WPU-ACT emulsions were diluted to 0.1 wt % and then mixed with different ratios. The mixing samples were denoted as D&M1:5, D&M2:4, D&M3:3, D&M4:2, and D&M5:1, and their particle size distributions were recorded in Figure 6B–D. It can be observed that particle sizes increased significantly after mixing at different ratios because they attracted each other after oppositely charged particles were in close proximity, forming larger particles. When blending anionic and cationic WPU-ACT with the same ratios (D&M3:3), the mixing samples exhibited the highest particle sizes.

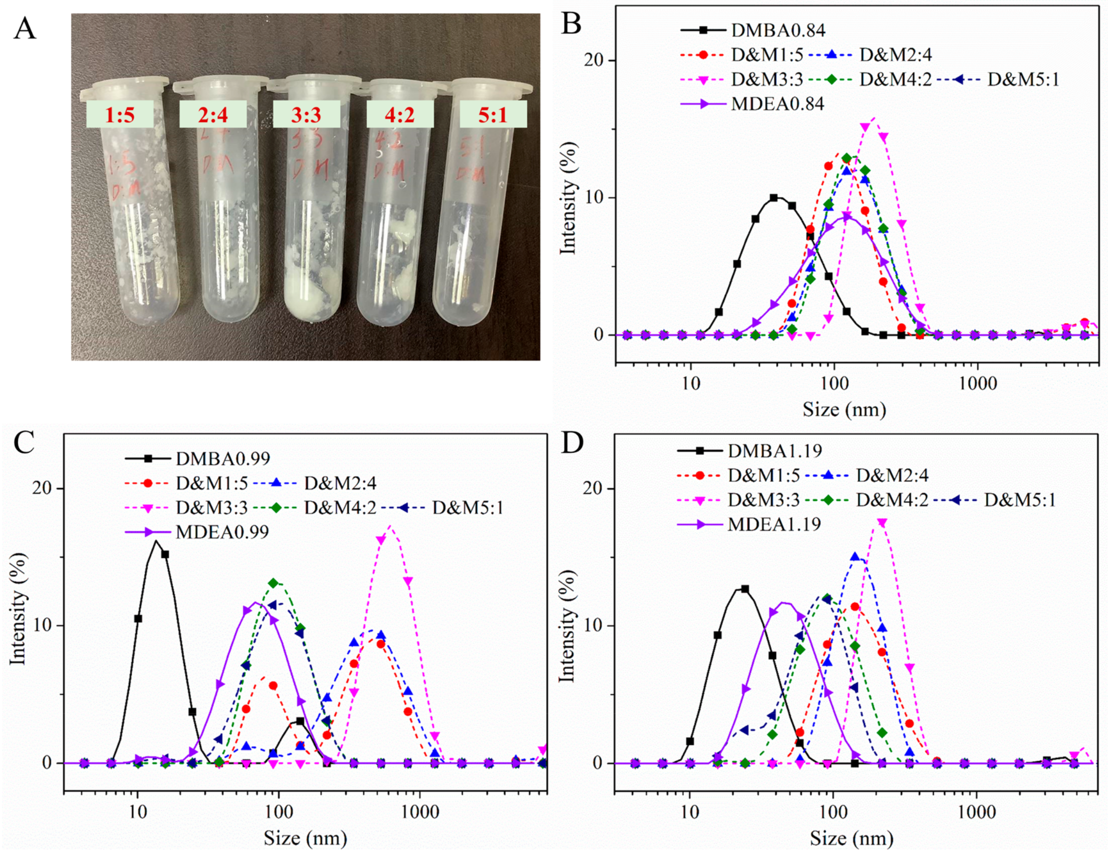

Figure 6. Mixing behavior of anionic and cationic WPU-ACT at different ratio (DMBA*n*:MDEA*n* = 1:5, 2:4, 3:3, 4:2, and 5:1). (A) Macroscopic phenomena of DMBA0.99 and MDEA0.99 emulsions (1 wt %) after mixing at different ratio. Particle size distribution of anionic and cationic WPU-ACT emulsions (0.1 wt %) after mixing for (B) DMBA0.84 and MDEA0.84, (C) DMBA0.99 and MDEA0.99, and (D) DMBA1.19 and MDEA 1.19.

Improving the resistance ability of pesticides to wash-off is another key factor for pesticide retention in spray applications. Herein, laboratory scale wash off experiments were performed for simulating the rain environment, and the rainfastness was studied following a literature-cited method;[42] the results are displayed in Figure 7. When anionic and cationic WPU-ACT formulations (D&M0.99) were simultaneously sprayed, the initial ACT concentration was 2.77 $\mu g/cm^2$, which was nearly twice that of a single spray of the ACT formulation. After the wash-off process, only 7.3% ACT retained on the ACT-T80-treated leaf surface, while 67.0%, 75.7%, and 87.9% of ACT retained for the DMBA0.99, MDEA0.99, and D&M0.99 formulations, respectively (Figure 7A). Also, multiple deposits or polymer membranes covered the rice foliar surfaces (Figure 7 C−F and C′-F′). After a water wash, most of the polymer membranes still remained on the leaves treated with DMBA0.99, MDEA0.99, and D&M0.99 formulations (Figure. 7 d−f and d′−f′), while scarcely any of the deposits of the ACT-T 80 formulation adhered on the leaves (Figure 7 c and c′). The strong rainfastness abilities of the WPU-ACT formulations were derived from the inherent adhesion stress of polyurethane to the material surface by polarity and hydrogen bond interactions.[19] All these results clearly established that the WPU-ACT formulations effectively improved the pesticide retention, especially the simultaneous spray of anionic and cationic WPU-ACT emulsions, which exhibited the strongest deposition and rainfastness abilities.

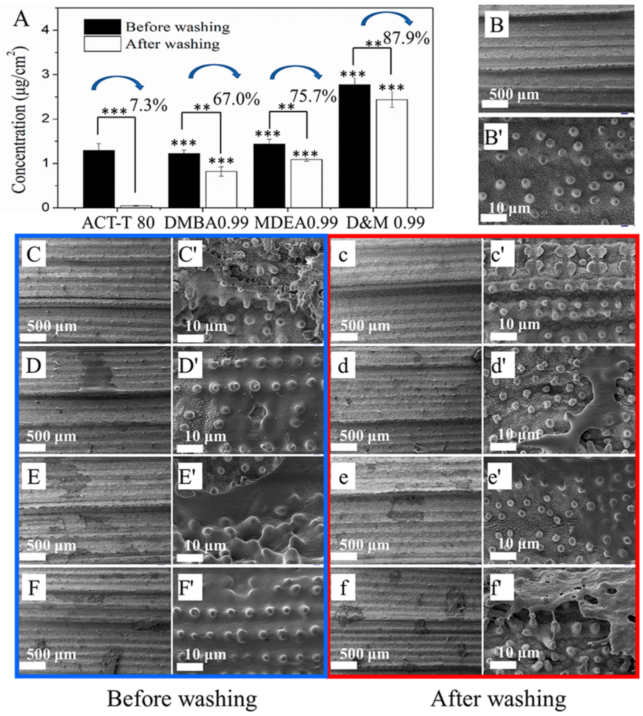

Figure 7. Rainfastness of different ACT formulations (0.1 wt % ACT). (A) The ACT concentration on rice leaves before and after washing; arrows represent the retention rate of ACT after washing. (B−F) SEM images of rice leaves sprayed with ACT formulations (C−F) before and (c-f) after washing (100 times). Panel B shows the blank rice leaf surface, panel C shows ACT-T80, panel D shows DMBA0.99, panel E shows MDEA0.99, and panel F shows D&M 0.99. Panels B′−F′ and c′−f′ are the magnified images (5000×). The statistical significance is $*p < 0.05$, $**p < 0.01$, and $***p < 0.005$.

To investigate whether the WPU-ACT formulations could prolong the pesticide retention and control pests in agriculture, the field efficiency of these formulations against the brown planthopper was measured with 0.3 mg/m^2 of ACT (Figure 8).

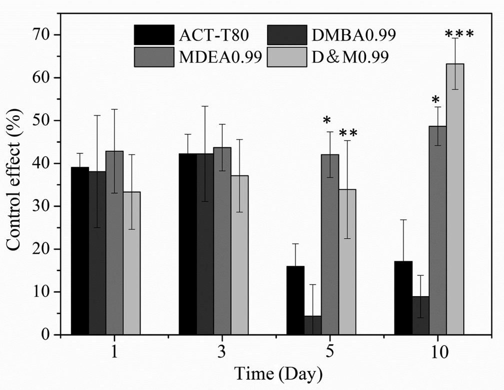

Figure 8. Field efficiency of different ACT formulations (0.3 mg/m^2 ACT) against the brown planthopper. The statistical significance is $*p < 0.05$, $**p < 0.01$, and $***p < 0.005$.

Showers occurred frequently during the experimental period. After spraying, all ACT formulations displayed no obvious difference in the control effect around 40% at the initial 3 days. However, on the fifth day the ACT-T80 and DMBA0.99 formulations exhibited almost no control effect, while MDEA0.99 and D&M0.99 still maintained the control effect and even higher effects because of the following two reasons: (1) the stability of ACT in the MDEA0.99 formulation was stronger under the sunlight than that in the ACT-T80 and DMBA0.99 formulations (Figure 3 D) and (2) there were frequent showers after spraying (Table S7). According to laboratory scale wash off experiments, the residual amount of ACT on rice surfaces treated with MDEA0.99 and D&M0.99 formulations after rainfall was much higher than that of surfaces treated with the ACT-T80 and DMBA0.99 formulations. The field efficacy assessment along with the stability test, release behavior, and deposition and wash off experiments confirmed that the WPU-ACT drug release system significantly improved the retention of ACT on the rice surface. As anionic WPU-ACT emulsions offered minimal protections for ACT due to the alkaline environment, they potentially can be used as a carrier for other pesticides that are stable in the alkaline environment. Additionally, oppositely charged WPU-ACT emulsions can be used as carriers of different synergistic pesticides and can be applied promisingly in modern agricultural formulations.

Since WPU-ACT emulsions are intended for food-based applications, the cytotoxicities of them and ACT were studied by the MTT assay, which was frequently applied to screen the polymer cytotoxicity for its reliability and sensitivity. As shown in Figure S4, the viability of African green monkey kidney cells (Marc-145) was higher than 90% after incubation for 24 and 48 h when all the WPU-ACT emulsions were diluted to less than 2500 $\mu g/mL$, which is much higher than their spray concentration (150 $\mu g/mL$) in the field efficiency. ACT (alone) showed no toxicity for the cells at concentrations lower than 500 $\mu g/mL$, which is also higher than its spray concentration (15 $\mu g/mL$) in the field efficiency test. These results indicated that the WPU-ACT samples could meet safety requirements for agricultural and food-based applications. It can be observed that the toxicity increases with ionic groups for the polyurethanes, resulting in the following order of toxicity: DMBA1.19 > DMBA0.99 > DMBA0.84. The low cell viability of WPU-ACT emulsions at a high concentration (5000 μg/mL) is probably caused by the inherent toxicity of nano systems[53] and the large amount of ammonium salts after neutralization. There is a lack of a complete understanding of nanomaterial toxicity and its impact on the human world. Some synthetic materials, such as poly(lactic-co-glycolic acid), polycaprolactone, or natural materials such as collagen or chitosan, with biodegradability could be used as nanoparticles in medical applications.[54] Waterborne polyurethanes in this study were prepared from natural vegetable oil, which could potentially be used in the agricultural field with little negative effects on the human body. The inherent toxicity of the nano WPU-ACT system will be studied in our future work. The more hydrophilic the chain extender in the polyurethane, the more ionic groups (ammonium salts) are formed after neutralization and hence the lower the cell viability of the corresponding WPU-ACT sample is.

CONCLUSIONS

In summary, a novel and environmentally friendly oppositely charged waterborne polyurethane-based drug delivery system with ACT loading was successfully prepared through a facile and economical method. Cationic WPU-ACT formulations displayed better sustained release behavior and excellent protective effects for ACT against light and heat. The simultaneous spray of anionic and cationic WPU-ACT significantly enhanced the spray deposition and rainfastness. A maximum retention ratio of 89% was obtained. A field efficacy assessment also indicated that the simultaneous spray of anionic and cationic WPU-ACTs effectively controlled brown planthoppers. Finally, it was demonstrated that these oppositely charged castor oil-based eco-friendly waterborne polyurethanes hold great promise in modern agricultural applications.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsami.0c10620.

> Preparation of the cytotoxicity assay; additional experimental data and parameters; and figures regarding pesticide spraying, surface tension of waterborne polyurethanes, curve fittings of release data, and cell viability (PDF)

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Notes

The authors declare no competing financial interest.

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