Hybrid Janus microparticles achieving selective encapsulation for theranostic applications via a facile solvent emulsion method

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2018

Lim, J. Y. G., Poh, W. K. C., & Loo, J. S. C. (2019). Hybrid Janus microparticles achieving selective encapsulation for theranostic applications via a facile solvent emulsion method. *Macromolecular Rapid Communications*, 40(7), 1800801-. doi:10.1002/marc.201800801

<https://hdl.handle.net/10356/144219>

<https://doi.org/10.1002/marc.201800801>

This is the accepted version of the following article: Lim, J. Y. G., Poh, W. K. C., & Loo, J. S. C. (2019). Hybrid Janus microparticles achieving selective encapsulation for theranostic applications via a facile solvent emulsion method. *Macromolecular Rapid Communications*, 40(7), 1800801-. doi:10.1002/marc.201800801, which has been published in final form at 10.1002/marc.201800801. This article may be used for non-commercial purposes in accordance with the Wiley Self-Archiving Policy [<https://authorservices.wiley.com/authorresources/Journal-Authors/licensing/self-archiving.html>].

Macromolecular Rapid Communications

Article Type - Communication Hybrid Janus Microparticles Achieving Selective Encapsulation for Theranostic Applications via a Facile Solvent Emulsion Method --Manuscript Draft--

Manuscript Number:	marc.201800801R1
Full Title:	Article Type - Communication Hybrid Janus Microparticles Achieving Selective Encapsulation for Theranostic Applications via a Facile Solvent Emulsion Method
Article Type:	Communication
Section/Category:	
Keywords:	controlled release; biodegradable; delivery systems; co-encapsulation; nanoparticles
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Abstract:	Anisotropic Janus particles composing of biocompatible polymers has been gaining considerable interest for biomedical applications. Here, we show the fabrication of hybrid Janus particles, via a single-step, solvent emulsion technique, potentially for theranostic purposes. Through this technique, we streamlined the selective encapsulation of therapeutic and diagnostic agents into different "faces" of the Janus structure. This facile technique could be used to seamlessly fabricate polymeric-based hybrid Janus particles for theranostic applications with little complexity.
Additional Information:	
Question	Response
Please submit a plain text version of your cover letter here.	<p>7 Dec 2018</p> <p>Dr Kirsten Severing Editor-in-Chief Macromolecular Rapid Communications</p> <p>Re: Revision of our Reviewed Manuscript Submitted to Macromolecular Rapid Communications - marc.201800801</p> <p>Dear Dr Severing,</p> <p>My co-authors and I would like to thank you for reviewing our manuscript entitled "Hybrid Janus Microparticles Achieving Selective Encapsulation for Theranostic Applications via a Facile Solvent Emulsion Method". In this revision, we have revised</p>

	<p>the manuscript according to the Reviewers' comments.</p> <p>We hereby state that this submission has not been published previously, that it is not under consideration for publication elsewhere, and that if accepted it will not be published elsewhere in the same form, in English or in any other language, without the written consent of the publisher.</p> <p>Any correspondences with regards to this submitted manuscript can be referred directly to me through email at joachimloo@ntu.edu.sg. Alternatively, I can also be contacted through telephone (+65 67904603) or fax (+65 67909081). My co-author and I would greatly appreciate if you could kindly re-review this article for publication in Macromolecular Rapid Communications.</p> <p>Thank you.</p> <p>Best Regards, Joachim Loo Associate Professor School of Materials Science and Engineering Nanyang Technological University 50 Nanyang Avenue, Singapore 639798 Email: joachimloo@ntu.edu.sg</p>
Do you or any of your co-authors have a conflict of interest to declare?	No. The authors declare no conflict of interest.

DOI: 10.1002/marc.((insert number)) ((or ppap., mabi., macp., mame., mren., mats.))

Article Type - Communication

Hybrid Janus **Microparticles** Achieving Selective Encapsulation for Theranostic Applications via a Facile Solvent Emulsion Method^a

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Anisotropic Janus particles composing of biocompatible polymers has been gaining considerable interest for biomedical applications. Here, we show the fabrication of hybrid Janus particles, via a single-step, solvent emulsion technique, potentially for theranostic purposes. Through this technique, we streamlined the selective encapsulation of therapeutic and diagnostic agents into different “faces” of the Janus structure. This facile technique could be used to seamlessly fabricate polymeric-based hybrid Janus particles for theranostic applications with little complexity.

^a **Supporting Information** is available online from the Wiley Online Library or from the author.

1 Introduction

The synthesis of Janus particles has gained considerable momentum over the recent few years particularly because of their versatility for myriad of applications.¹ The asymmetry of these structurally unique particles endow them with characteristics suitable for drug delivery, controlled release, diagnostics and even in self-assembly systems.^{2, 3} Through surface deposition techniques, inorganic Janus particles can be fabricated by partial coating of the exposed face with a functional material, while leaving the underside uncoated. For example, Guix et al. created effervescent-driven asymmetric particles by partially coating calcium carbonate microparticles with platinum and successfully demonstrated non-Brownian movement of these particles in an acidic tumour environment⁴.

Another popular technique for Janus particle fabrication is through Pickering emulsions, whereby the adsorption of particles at the interface between two immiscible fluids allows for selective modification of their surfaces to produce anisotropic properties. For example, Jiang et al. reported the use of silica-based, amphiphilic Janus particles fabricated through Pickering emulsions to achieve emulsions with colloidal stabilities beyond three weeks.⁵ Despite these efforts, these techniques usually require strictly-controlled multi-steps processes. In addition, the high processing temperatures and solvents required to remove the masking layer for Pickering emulsions is generally unsuitable for biodegradable polymers.⁶ Furthermore, these methods have limitations for drug encapsulation in controlled release applications.

While inorganic Janus particles have shown to be promising for biomedical applications, polymeric Janus particles have similarly garnered considerable interest due to the greater flexibility in fabricating these organic-based structures through simpler and more convenient processes.⁷ Polymeric Janus particle fabrication has predominantly been

carried out through polymerization, microfluidics, and solvent evaporation techniques⁸.

For microfluidics, two different polymers are co-extruded through two channels that meet at a single junction, creating a precipitated droplet with two distinct faces.²

However, microfluidics requires specific control and are limited by low output efficiencies. Furthermore, polymer solutions for microfluidics fabrication have to be of low viscosities with specific viscoelastic responses, hence limiting the choice of polymers.⁹ Other methods like electrohydrodynamic co-jetting have also been shown to be capable of fabricating drug-loaded polymeric Janus particles.¹⁰

To address to the above challenges, a facile approach to consistently fabricate polymeric Janus particles via the solvent emulsion technique was thus employed. While the use of solvent emulsions for the fabrication of Janus particles has been reported, most efforts for drug encapsulation primarily focused on PLGA and solid lipids¹¹ as the main composition materials. Solid lipids have short shelf-lives, which could affect its stability and duration of compatible use with more stable polymers, such as PLGA.¹² In our previous work, it was shown that the loading of drugs into Janus particles via solvent emulsion could affect the final structure of the particle, i.e. Janus, core-shell, etc..¹³ Hence, we wanted to further build upon this knowledge to investigate how this technique can also allow for co-encapsulation of drugs and other inorganic nanoparticles, without compromising on its structure, and how co-encapsulation can influence drug release kinetics.

Our intent is to report on the synthesis of dual drug-loaded, theranostic Janus particles, using a single-step solvent evaporation emulsion, composing of different polymer combinations – biodegradable with non-biodegradable. Such a technique would subsequently allow for an economical, seamless and scalable approach towards

developing multi-drug-loaded Janus particles with controlled release capabilities. This scalable one-pot process of creating theranostic Janus particles that combines drug encapsulation and theranostic nanomaterials into a single entity to elicit different drug release kinetics while possessing other biomedical functions has, to the best of our knowledge, not been reported.

2 Results and Discussion

2.1 Synthesis of dual drug-loaded Janus particles with different polymers

A combination of biocompatible and widely used polymers were chosen for the fabrication of Janus particles, namely the biodegradable aliphatic polyesters, i.e. PLGA, poly (lactic acid) (PLLA), together with the non-biodegradable poly(methyl methacrylate) (PMMA) and poly (ethyl vinyl acetate) (EVA). Upon emulsification with an overhead stirrer, the immiscible polymer phases in a polymer solution spontaneously segregate into two separate faces. This is due to the interfacial tensions of the three phases (i.e. both dissolved polymers in the organic phases and the aqueous phase) fulfilling specific interfacial interactions.¹³ **Table S1** shows the the weight ratios required to fabricate the different polymeric combinations of Janus particles. Interfacial tension studies were done to validate the thermodynamic requirements to achieve Janus particles (**Table S2**).

(Figure 1)

Figure 1a-c shows the respective images of the Janus particles, evident from the distinct line separating both polymer faces. The yields for all these Janus structures were determined to be ~ 100%. The use of high molecular weight PLLA (I.V. 2.36) here also validates the ability to fabricate Janus particles using polymers of relatively high viscosities, which is a limitation of microfluidics (**Figure 1c**).¹⁴

The encapsulation of Dox, as a drug, into these Janus particles was subsequently investigated.

Figure 1d-f shows the optical images of Dox-loaded Janus particles. The luminiscence red of Dox¹⁵ was observed on only one side of the Janus particle – either PLGA or PLLA. Selective dissolution of EVA from Dox-loaded EVA/PLGA and EVA/PLLA Janus particles gave undissolved red half-crescents that were subsequently determined to be PLGA and PLLA, respectively. Likewise, for PMMA/PLGA Janus particles, transparent (i.e. absence of Dox) half-crescents of PMMA remained through selective dissolution of PLGA, which proved the selective compartmentalization of Dox in PLGA (**Figure S1**).

From previous studies, it was shown that polymer-drug interaction is an important factor in designing drug-loaded particles.¹⁶ In addition, we postulated that hydrophilic affinity between PLGA and Dox also played a role in driving this selective localization. Contact angles, as a representation of degree of hydrophilicity, of these polymers were measured (**Figure S2**). The results validates that the aliphatic polyesters are generally more hydrophilic compared to the non-biodegradable polymers, thus providing preferential loading of Dox into the polyesters.

Next, two therapeutics of disparate solubilities were encapsulated into these Janus particles. The idea of selective drug encapsulation into different ‘faces’ mitigates undesirable drug-to-drug interactions, while allowing for the release kinetics of each drug to be determined by its encapsulant polymer. This also reduces the complexity of clinically administering two polymer particle batches simultaneously.^{2, 17} Paclitaxel (PTX) was chosen along with Dox because of their solubility difference (logP values of 0.71¹⁸ and 3.96¹⁹, respectively), and for their well-studied synergistic effects in cancer therapy²⁰. Based on encapsulation efficiency calculations (EE%) (**Table S3-4**), the EE% of Dox (>85%) was higher than loading into single polymer particles.

From **Table S4**, it is shown that the % loading of PTX into EVA for EVA/PLGA particles was the highest (86% in EVA and 14% in PLGA), whilst the loading % of PTX reduced to 69% for EVA/PLLA (31% in PLLA), and 45% for PMMA/PLGA (55% in PLGA). As PLLA is deemed to be a relatively more hydrophobic polymer to PLGA, arising from the methyl groups along its backbone²¹, some appreciable partitioning of hydrophobic PTX into PLLA would occur. For PMMA/PLGA Janus particles, the loading % of PTX appears to be relatively equal in both compartments, inferring that both PLGA and PMMA exhibited similar degree of interaction with PTX, thus resulting in a more equitable distribution. These results again correlated well with the respective contact angle measurements for each individual polymer (**Figure S2**), with more hydrophobic polymers encapsulating a higher proportion of PTX. While this validates our initial hypothesis and prediction of how selective drug encapsulation can be achieved through drug-polymer interactions,²² this also provides the means to tune the loading % distribution of PTX within Janus particles through the use of different polymers.

2.2 Drug Release Studies

Drug release studies were conducted until 100% release of either drug was achieved. Release rates were determined through calculations of their release kinetics and corresponding correlation coefficients, using the Higuchi model (**Table S5**). Only the release kinetics of PTX from PMMA/PLGA was not calculated due to insufficient release (< 20 %) across the entire release period. The release of Dox through diffusion, had similar rate constants of $5.7 \pm 0.4 \text{ h}^{-1}$ for all three Janus particles ($R^2 > 0.99$).

(**Figure 2**)

PTX, on the other hand, displayed contrasting release kinetics from all three Janus particles. A descending order of PTX release was observed from EVA/PLGA, EVA/PLLA to PMMA/PLGA. Based on the drug loading % (**Table S4**), we envisaged that the release of PTX from EVA/PLGA would largely be from EVA due to its higher loading % of PTX (~85%). On

the other hand, the release of PTX from PMMA/PLGA will likely be from both faces given their almost equal distribution.

From release studies of single-polymer microparticles of similar sizes (100 – 120 μm) (**Figure S3**), the release of PTX was fastest from EVA and descending from PLGA, PLLA to PMMA. As PTX was mostly encapsulated in EVA (86%) for EVA/PLGA, its release kinetics closely mimics that of PTX release from EVA alone. In fact, the summation of the release amount based on proportional drug loading % from single polymers was found to equate that of PTX release from EVA/PLGA Janus particles (**Figure S3**). As for EVA/PLLA and PMMA/PLGA, their release closely mimics that of PTX release from individual polymers with the corresponding proportion of % drug loading. The release of PTX from Janus particles is therefore determined by the % of PTX in the encapsulant polymer and the release property of the individual encapsulant polymer.

From a dual-drug release perspective, the results suggest that different release kinetics of Dox relative to PTX can therefore be achieved from Janus particles. EVA/PLGA Janus particles (**Figure 2a**) can provide a simultaneous release (i.e. similar rates) of both drugs (**Table S5**), while a sequential release of Dox followed by PTX can be realized through PMMA/PLGA Janus particles. This validates how Janus particles, through the use of different polymers, can achieve differing release kinetics of hydrophobic drugs, such as as PTX.

2.3 Functionalization of drug-loaded hybrid Janus Particles

2.3.1 For targeting and bioimaging

In previous studies, various groups have incorporated inorganic magnetic materials into Janus particles with targeting or diagnostic (i.e. MRI) properties.²³ Superparamagnetic iron oxides nanoparticles (SPIONs) are promising nanomaterials as magnetic resonance imaging (MRI) contrast agents due to their known biocompatibility and ease of fabrication²⁴. To endow

polymeric Janus particles with these properties, SPIONs were incorporated seamlessly during the solvent emulsion synthesis. SPIONs functionalized with oleic acid was added into a dual drug-loaded (i.e. Dox and PTX) polymer solution of EVA/PLGA, EVA/PLLA and PMMA/PLGA before further emulsification. It was observed that SPIONs localized into the aliphatic polyesters for all the Janus particle combinations (**Figure 3f-h.**), as determined through selective dissolution (**Figure S1**). From **Figure 3b**, SPIONs-loaded Janus particles were shown to possess magnetically-driven mobility through the influence of a magnetic source demonstrating the potential of these hybrid Janus particles for magnetic targeting or even bioimaging.

(Figure 3)

The partitioning of SPIONs into the biodegradable aliphatic polyesters led us to investigate its encapsulation into individual polymer particles. It was observed that the encapsulation of SPIONs was possible for all single-polymer particles, even though preferential partitioning of SPIONs was observed for Janus particles. The extent of hydrogen bonding between the water droplet and the surface of the respective polymers influences the contact angle (**Figure S2**).²⁵ Stronger hydrogen bonding between PLGA and H₂O reduces the surface tension within the water droplet, and decreases contact angle. The surface of SPIONs fabricated via co-precipitation, in an aqueous medium, gives rise to exposed hydrophilic hydroxyl groups thus promoting hydrogen bonding.²⁶ These SPIONs would therefore have an increasing degree of hydrogen bonding in the order of EVA<PMMA<PLLA<PLGA, resulting in the selective encapsulation within the aliphatic polyesters.

2.3.2 For selective surface coating

Besides encapsulation, selective functionalized surface coating of Janus particles was also investigated through this seamless, one-step solvent emulsion technique, whereby calcium phosphate (CaP) – an inorganic bone mineral, was coated onto one of the ‘face’ of the Janus

particles. **Figure 4a** shows CaP coating onto one side of the Janus particle. **Figure 4b** shows the EDX overlay mapping of the same particle with the elemental mapping of both Ca and P in the overlay on one side of the Janus particle, against a contrast on the other side. A hybrid Janus particle could therefore potentially allow for further surface modification using ligands such as bisphosphonates to endow these particles with bone targeting capabilities ²⁷.

To validate the robustness of this technique, selective coating of CaCO₃ was also explored. Partially coated Janus particles with CaCO₃ can be developed into micro-motors when exposed to a lightly acidic medium²⁸. Here, ammonium dihydrogen phosphate was replaced with ammonium bicarbonate to precipitate CaCO₃ onto the Janus particle. From **Figure 4c**, CaCO₃ was precipitated onto the EVA face of the EVA/PLGA Janus particle, which was confirmed with EDX (**Figure 4d**). Images showing multiple selectively coated particles and their respective EDX images are shown in **Figure S4**. This shows the capability of this technique to selectively functionalize these particles at a high yield and at greater convenience.

4. Conclusions

Dual-drug Janus microparticles can be seamlessly fabricated through a facile solvent emulsion method with the use of biocompatible polymers in specific ratios, while allowing for selective drug localization. Drug localization within the Janus particles is influenced by polymer-drug interaction. The hydrophilic drug Dox was observed to be encapsulated in the aliphatic polyesters, while hydrophobic PTX was partitioned between both polymers that is dependent on their hydrophilicities. Because of this, release kinetics of PTX from Janus particles can be tuned. In addition, this seamless technique allows for the selective encapsulation and surface coating of SPIONs and calcium-based ceramics respectively, for potential theranostic applications. While the use of large particles may restrict their route of administration (e.g. intravenous, pulmonary), these particles may still be suitable for controlled release in oral,²⁹

intraperitoneal,³⁰ and subcutaneous delivery as a drug depot,³¹ and in skin wound applications.³²

In addition, the use of Janus particles would trump the use of single-drug loaded particles because of the requirement of just one synthesis setup for co-encapsulation in Janus particles.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author

Acknowledgements

The authors would like to acknowledge the financial support from the Singapore Centre for Environmental Life Sciences Engineering (SCELSE) (MOE/RCE: M4330019.C70), the School of Materials Science and Engineering (M020070110), the Ministry of Education AcRF-Tier 1 grant (RG19/18), and the NTU-HSPH grant (NTU-HSPH 17002).

Conflict of Interest

The authors declare no conflict of interest.

Keywords

controlled release, biodegradable, delivery systems, co-encapsulation, biocompatible, nanoparticles

1. Hu, J.; Zhou, S.; Sun, Y.; Fang, X.; Wu, L., *Chemical Society Reviews* **2012**, 41 (11), 4356-4378.
2. Xie, H.; She, Z.-G.; Wang, S.; Sharma, G.; Smith, J. W., *Langmuir: the ACS journal of surfaces and colloids* **2012**, 28 (9), 4459.
3. Kumar, A.; Park, B. J.; Tu, F.; Lee, D., *Soft Matter* **2013**, 9 (29), 6604-6617.
4. Guix, M.; Meyer, A. K.; Koch, B.; Schmidt, O. G., *Scientific reports* **2016**, 6.
5. Jiang, S.; Chen, Q.; Tripathy, M.; Luijten, E.; Schweizer, K. S.; Granick, S., *Advanced materials* **2010**, 22 (10), 1060-1071.
6. Passas-Lagos, E.; Schuth, F., *Langmuir* **2015**, 31 (28), 7749-7757.
7. Lone, S.; Cheong, I. W., *Rsc Advances* **2014**, 4 (26), 13322-13333.
8. Wurm, F.; Kilbinger, A. F., *Angewandte Chemie International Edition* **2009**, 48 (45), 8412-8421.

9. Abate, A. R.; Kutsovsky, M.; Seiffert, S.; Windbergs, M.; Pinto, L. F.; Rotem, A.; Utada, A. S.; Weitz, D. A., *Advanced materials* **2011**, 23 (15), 1757-1760.
10. Hwang, S.; Lahann, J., *Macromolecular rapid communications* **2012**, 33 (14), 1178-1183.
11. Garbuzenko, O. B.; Winkler, J.; Tomassone, M. S.; Minko, T., *Langmuir* **2014**, 30 (43), 12941.
12. Naseri, N.; Valizadeh, H.; Zakeri-Milani, P., *Advanced pharmaceutical bulletin* **2015**, 5 (3), 305.
13. Fan, Y. L.; Tan, C. H.; Lui, Y.; Zudhistira, D.; Loo, S. C. J., *RSC Advances* **2018**, 8 (29), 16032-16042.
14. Perry, S. L.; Higdon, J. J.; Kenis, P. J., *Lab on a Chip* **2010**, 10 (22), 3112-3124.
15. Lewis, A. L.; Taylor, R. R.; Hall, B.; Gonzalez, M. V.; Willis, S. L.; Stratford, P. W., *Journal of vascular and interventional radiology* **2006**, 17 (8), 1335-1343.
16. Mistry, P.; Mohapatra, S.; Gopinath, T.; Vogt, F. G.; Suryanarayanan, R., *Molecular pharmaceutics* **2015**, 12 (9), 3339-3350.
17. Romanski, F. S.; Winkler, J. S.; Riccobene, R. C.; Tomassone, M. S., *Langmuir* **2012**, 28 (8), 3756-3765.
18. Neubert, A.; Sternberg, K.; Nagel, S.; Harder, C.; Schmitz, K.-P.; Kroemer, H. K.; Weitschies, W., *Journal of Controlled Release* **2008**, 130 (1), 2-8.
19. Surapaneni, M. S.; Das, S. K.; Das, N. G., *ISRN pharmacology* **2012**, 2012.
20. Lee, W. L.; Guo, W. M.; Ho, V. H.; Saha, A.; Chong, H. C.; Tan, N. S.; Widjaja, E.; Tan, E. Y.; Loo, S. C. J., *Small* **2014**, 10 (19), 3986-3996.
21. Makadia, H. K.; Siegel, S. J., *Polymers* **2011**, 3 (3), 1377-1397.
22. Rahman, N.; Mathiowitz, E., *Journal of controlled release* **2004**, 94 (1), 163-175.
23. Zenerino, A.; Peyratout, C.; Aimable, A., *Journal of colloid and interface science* **2015**, 450, 174-181.
24. Qiao, R.; Yang, C.; Gao, M., *Journal of Materials Chemistry* **2009**, 19 (35), 6274-6293.
25. Zheng, W.; Sun, C.; Bai, B., *Polymers* **2017**, 9 (8), 370.
26. Rehana, D.; Haleel, A. K.; Rahiman, A. K., *Journal of Chemical Sciences* **2015**, 127 (7), 1155-1166.
27. Bastari, K.; Arshath, M.; Ng, Z. H. M.; Chia, J. H.; Yow, Z. X. D.; Sana, B.; Tan, M. F. C.; Lim, S.; Loo, S. C. J., *Journal of materials science: Materials in medicine* **2014**, 25 (3), 747-757.
28. Guix, M.; Meyer, A. K.; Koch, B.; Schmidt, O. G., *Scientific reports* **2016**, 6, 21701.
29. Baek, J.-S.; Tee, J. K.; Pang, Y. Y.; Tan, E. Y.; Lim, K. L.; Ho, H. K.; Loo, S. C. J., *Neuromolecular medicine* **2018**, 1-9.
30. Baek, J.-S.; Choo, C. C.; Tan, N. S.; Loo, S. C. J., *Oncotarget* **2017**, 8 (46), 80841.
31. McLennan, D. N.; Porter, C. J.; Charman, S. A., *Drug Discovery Today: Technologies* **2005**, 2 (1), 89-96.
32. Wang, X.; Sng, M. K.; Foo, S.; Chong, H. C.; Lee, W. L.; Tang, M. B. Y.; Ng, K. W.; Luo, B.; Choong, C.; Wong, M. T. C.; Tong, B.M.K.; Chiba, S.; Loo, S. C. J.; Zhu, P. C.; Tan, N.S., *Journal of Controlled Release* **2015**, 197, 138-147.

Figure 1. (a) EVA/PLGA, (b) PMMA/PLGA, (c) EVA/PLLA Janus particles, (d) EVA/PLGA + Dox, (e) PMMA/PLGA + Dox, (f) EVA/PLLA + Dox.

Figure 2. Release studies of Dox and PTX for (a) EVA/PLGA, (b) EVA/PLLA, (c) PMMA/PLGA Janus particles.

Figure 3. (a) Schematic of SPION encapsulation in polymeric Janus particles, (b) Magnetic behavior of drug and SPIONs loaded EVA/PLGA Janus particles (c-f) SPION encapsulation in PLLA, EVA, PLGA and PMMA, (g) EVA/PLLA, (h) EVA/PLGA, (i) PMMA/PLGA Janus particles encapsulated with SPIONs.

Figure 4. (a) SEM image of CaP onto one side of the EVA/PLGA particle, (b) EDX overlay image of the same EVA/PLGA Janus particle coated with CaP, with the calcium and phosphorous compounds in green and red respectively, (c) SEM image of CaCO₃ coated onto one side of the EVA/PLGA Janus particle (d) EDX image of the EVA/PLGA Janus particle showing the contrast of calcium on the same side as the precipitates seen (e) Light microscope image of the CaCO₃ precipitates on the EVA of the EVA/PLGA Janus particles

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Hybrid Janus Particles Achieving Selective Encapsulation for Theranostic Applications via a Facile Solvent Emulsion Method

Polymeric Janus Particles equipped with drug delivery, targetable capability as well as functionalized surface anisotropy can be fabricated through a simple one-pot solvent emulsion synthesis. Janus particles of different polymeric combinations fabricated in this method show unique drug release profiles, allowing for synergistic drug release in a myriad of ways.

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