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Oriented, molecularly imprinted cavities with dual binding sites for highly sensitive and selective recognition of cortisol

Narito Suda, Hirobumi Sunayama, Yukiya Kitayama, Yuri Kamon and Toshifumi Takeuchi

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Review timeline

Original submission: 4 April 2017

Revised submission: 12 July 2017

Final acceptance: 18 July 2017

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

Review History

RSOS-170300.R0 (Original submission)

Review form: Reviewer 1 (Shengchang Xiang)

Is the manuscript scientifically sound in its present form?

Yes

Are the interpretations and conclusions justified by the results?

Yes

Is the language acceptable?

Yes

Is it clear how to access all supporting data?

Yes

Do you have any ethical concerns with this paper?

No

Have you any concerns about statistical analyses in this paper?

No

Recommendation?

Accept with minor revision (please list in comments)

Comments to the Author(s)

This manuscript reports the study on high selectivity and sensitivity fluorescent sensing cortisol based on a competitive binding assay using a fluorescent competitor with molecularly imprinted polymers. The approach that developed in this article is interesting, fluorescent chemosensor was designed based on the using of a cortisol motif template molecule (TM1) which consists of a polymerizable moiety attached at the 3-carbonyl group of cortisol via an oxime linkage and an adamantane carboxylate moiety. The results show that this proposed approach can be successfully applied to detect cortisol in real samples, and a feasibility study in detection of cortisol in saliva samples. The work will be suitable for publication after addressing the following point:

1. The manuscript is essentially well written, but the language still needs some revising and polishing. Such as, in page 15 lines 21-22, the word of "the" should be removed.
2. The authors proposed the homogeneous cavities with two binding sites for cortisol, but there is no data to prove the formation of oxime bond. Please provide the FT-IR data to confirm it was formed.
3. The ref 32 is the same as ref 47, please check.
4. Authors need to include important references of the novel molecularly imprinted polymers with superior sensing performance. (i.e. *New J. Chem.* 2016, 40, 1649; *Monatsh Chem* 2015,146, 485; *J. Applied Polymer Sciences*, 2014, 131, 40491; *RSC Adv.*, 2013, 3, 25396)

Review form: Reviewer 2 (Adam McCluskey)**Is the manuscript scientifically sound in its present form?**

Yes

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Yes

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Yes

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Do you have any ethical concerns with this paper?

No

Have you any concerns about statistical analyses in this paper?

No

Recommendation?

Accept with minor revision (please list in comments)

Comments to the Author(s)

This is a well crafted paper from an established group in the MIP field. the experiments conducted are logical and well described in the text and at each point where this reviewer

thought that additional experiments should have been performed they were next described in the text. That is not to say that additional discussion / work is not warranted.

In many aspects this paper is comprehensive in its own right to be published as is, but this reviewer feels that an already strong body of work could be further enhanced with the inclusion of:

NMR data to validate the assertion that the adamantane moiety does indeed bind within the cyclodextrin moiety.

The inclusion of data on the cortisol concentration in human saliva based on an accredited approach - how does the MIP approach compare with the current best practice?

The paper would also benefit from the inclusion of a detailed list of abbreviations as at times it took multiple readings to determine what was actually being discussed.

While the selectivity data shown in graphical format is impressive and clearly details the key points of this work, researchers in the MIP field are used to examination of selectivity through impact factors etc.

Decision letter (RSOS-170300)

23-Jun-2017

Dear Professor Takeuchi:

Title: Oriented, Molecularly Imprinted Cavities with Dual Binding Sites for Highly Sensitive and Selective Recognition of Cortisol

Manuscript ID: RSOS-170300

Thank you for submitting the above manuscript to Royal Society Open Science. On behalf of the Editors and the Royal Society of Chemistry, I am pleased to inform you that your manuscript will be accepted for publication in Royal Society Open Science subject to minor revision in accordance with the referee suggestions. Please find the reviewers' comments at the end of this email.

The reviewers and handling editors have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the comments and revise your manuscript.

Because the schedule for publication is very tight, it is a condition of publication that you submit the revised version of your manuscript within 7 days (i.e. by the 02-Jul-2017). I note that some additional characterisation data has been requested, which you may need additional time to collect, so if you do not think you will be able to meet this date please let me know as soon as possible.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/rsos> and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions". Under "Actions," click on "Create a Revision." You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript and upload a new version through your Author Centre.

When submitting your revised manuscript, you will be able to respond to the comments made by the referees and upload a file "Response to Referees" in "Section 6 - File Upload". You can use this to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the referees.

When uploading your revised files please make sure that you have:

- 1) A text file of the manuscript (tex, txt, rtf, docx or doc), references, tables (including captions) and figure captions. Do not upload a PDF as your "Main Document".
- 2) A separate electronic file of each figure (EPS or print-quality PDF preferred (either format should be produced directly from original creation package), or original software format)
- 3) Included a 100 word media summary of your paper when requested at submission. Please ensure you have entered correct contact details (email, institution and telephone) in your user account
- 4) Included the raw data to support the claims made in your paper. You can either include your data as electronic supplementary material or upload to a repository and include the relevant doi within your manuscript
- 5) All supplementary materials accompanying an accepted article will be treated as in their final form. Note that the Royal Society will neither edit nor typeset supplementary material and it will be hosted as provided. Please ensure that the supplementary material includes the paper details where possible (authors, article title, journal name).

Supplementary files will be published alongside the paper on the journal website and posted on the online figshare repository (<https://figshare.com>). The heading and legend provided for each supplementary file during the submission process will be used to create the figshare page, so please ensure these are accurate and informative so that your files can be found in searches. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI.

Once again, thank you for submitting your manuscript to Royal Society Open Science. The chemistry content of Royal Society Open Science is published in collaboration with the Royal Society of Chemistry. I look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Best wishes,

On behalf of the Subject Editor Dr Anthony Stace and the Associate Editor Professor Claire Carmalt.

RSC Associate Editor:
Comments to the Author:
(There are no comments.)

RSC Subject Editor:
Comments to the Author:
(There are no comments.)

Reviewer comments to Author:

Reviewer: 1

Comments to the Author(s)

This manuscript reports the study on high selectivity and sensitivity fluorescent sensing cortisol based on a competitive binding assay using a fluorescent competitor with molecularly imprinted polymers. The approach that developed in this article is interesting, fluorescent chemosensor was designed based on the using of a cortisol motif template molecule (TM1) which consists of a polymerizable moiety attached at the 3-carbonyl group of cortisol via an oxime linkage and an adamantane carboxylate moiety. The results show that this proposed approach can be successfully applied to detect cortisol in real samples, and a feasibility study in detection of cortisol in saliva samples. The work will be suitable for publication after addressing the following point:

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Reviewer: 2

Comments to the Author(s)

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The paper would also benefit from the inclusion of a detailed list of abbreviations as at times it took multiple readings to determine what was actually being discussed.

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Author's Response to Decision Letter for (RSOS-170300)

See Appendix A.

Decision letter (RSOS-170300.R1)

18-Jul-2017

Dear Professor Takeuchi,

Title: Oriented, Molecularly Imprinted Cavities with Dual Binding Sites for Highly Sensitive and Selective Recognition of Cortisol
Manuscript ID: RSOS-170300.R1

It is a pleasure to accept your manuscript in its current form for publication in Royal Society Open Science. The chemistry content of Royal Society Open Science is published in collaboration with the Royal Society of Chemistry.

Thank you for your fine contribution. On behalf of the Editors of Royal Society Open Science and the Royal Society of Chemistry, I look forward to your continued contributions to the Journal.

Yours sincerely,

Liisa Niitsoo
Publishing Editor, Journals
Royal Society Open Science
Royal Society of Chemistry
Tel +44 (0) 1223 432167
chemistryopenscience@rsc.org

On behalf of the Subject Editor Professor Anthony Stace and the Associate Editor Professor Claire Carmalt.

RSC Associate Editor
Comments to the Author:
(There are no comments.)

Appendix A

Downloaded from <http://rsos.royalsocietypublishing.org/> on May 20, 2018

Response to reviewers

Reviewer 1

Q1-1. The manuscript is essentially well written, but the language still needs some revising and polishing. Such as, in page 15 lines 21-22, the word of "the" should be removed.

A1-1 Page 12, Line 16

We have proofread the whole manuscript and edited the sentences at page13, line 16 to 20.

Q1-2. The authors proposed the homogeneous cavities with two binding sites for cortisol, but there is no data to prove the formation of oxime bond. Please provide the FT-IR data to confirm it was formed.

A1-2 Figure 2

Unfortunately, any FI-IR data were not obtained due to the nm-sized thickness of the MIP, however, because MIP bearing the dual interaction sites (β -CD and aminoxy group) showed a greater affinity for cortisol the reference polymer RP- β -CD bearing single interaction site (β -CD), the aminoxy group in MIP can interact with cortisol.

Q1-3. The ref 32 is the same as ref 47, please check.

A1-3. The reference number was incorrect, and is has been corrected and re-numbered.

Q1-4. Authors need to include important references of the novel molecularly imprinted polymers with superior sensing performance. (i.e. New J. Chem. 2016, 40, 1649; Monatsh Chem 2015,146, 485; J. Applied Polymer Sciences, 2014, 131, 40491; RSC Adv., 2013, 3, 25396)

A1-4. The reviewer's suggested references have been cited in main text.

Reviewer 2

Q2-1. NMR data to validate the assertion that the adamantane moiety does indeed bind within the cyclodextrin moiety.

A2-1. Page 6, Lines 9 and Figure S1 in Supporting Information

We have conducted the additional experiments on the interaction between TM1 and β -CD, and added the following sentence in the main text at page 6, lines 9 to11, and Figure S1 in Supporting Information , "The interaction between β -CD and the adamantane group of TM1 was confirmed by ¹H-NMR (Fig. S1), while no interaction was observed between β -CD and the styryl group of TM1."

Q2-2. The inclusion of data on the cortisol concentration in human saliva based on an accredited approach - how does the MIP approach compare with the current best practice?

A2-2. Page 13, Lines 9

We have added the following phrase to the main text at page 13, lines 9 to 10, "where the detectability is comparable to that of commercially available ELISA [63] and radioimmuneassay [64]".

Q2-3. The paper would also benefit from the inclusion of a detailed list of abbreviations as at times it took multiple readings to determine what was actually being discussed.

A2-3. Page 17, Lines 12

The abbreviation list has been added in the main text at page 17, lines 12 to page 18, line 11.

Q2-4. While the selectivity data shown in graphical format is impressive and clearly details the key points of this work, researchers in the MIP field are used to examination of selectivity through impact factors etc.

A2-4. Page 12, Lines 1

We have added the key figures of the selectivity factors in the main text at page 12, line 1 to line 8.