

Arif Rahman Nurdianto didins99@gmail.com

Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: nanik-z@fkg.unair.ac.id

----- Forwarded message -----

Dari: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Sel, 8 Nov 2022 16.44

Subject: Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: Arif Rahman Nurdianto <didins99@gmail.com>

----- Forwarded message -----

From: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Mon, Nov 7, 2022, 16:03

Subject: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: <m.luthfi@fkg.unair.ac.id>

Dear Authors,

Thank you for submitting your article entitled: "**Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction**"

Based on our author guidelines, Your article fulfilled the minimum required structure,

<https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidelines>

In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive (<https://www.balimedicaljournal.org/index.php/bmj/issue/archive>).

According to the new International regulation, please fulfill the requirements below:

1. Ethical clearance number/statement and/or informed consent at the end of the manuscript (**Confirmed**).
2. Please state your conflict of interest in the paper. (**Confirmed**)
3. Please state the funding (if any) in your paper. (**Unconfirmed**)
4. Please state each author's contribution. (**Confirmed**)
5. Numerous grammatical errors were found in the text.

Please fulfill the unconfirmed statement above in the manuscript. Your article has been accepted to publish in our journal with minor revision. The article also has been processed by our editing partner REVISE as per instruction from our executive editor. Therefore, please complete the payment of the APC and the associated fee, so we can proceed to publish your article (Invoice attached). Your LoA will be sent as soon as we confirm your payment and please send us your proof of payment.

Best regards,
Editorial Team BaliMedJ

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)



Bali Medical Journal Worthy of Publication

Managing Editor:

editor@balimedicaljournal.org

editorbalimedicaljournal@gmail.com

<http://balimedicaljournal.org>

Invoice no: 3874/BMJ/14102022

Invoice date: **November 2022**

Recent Status: **Unpaid**

Valid until: November 10th 2022

Bill to: Muhammad Luthfi (m.luthfi@fkg.unair.ac.id)

Description	Quantity	Price	Amount
Basic Administration and Article Processing Charge (APC): "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 1000	USD 1000
Proofread and reviewing of Manuscript entitled: "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 100	USD 100
Subtotal			USD 1100
Total (Tax 0.5%)			USD 1105

*Note: please kindly adopt USD exchange to IDR day per day at the mean time you pay the respective APC.

All of the payment can be transferred to Indonesian Bank Account:

Jenius (BTPN): Sintisarisains

or

Bank Syariah Indonesia (BSI): 7099787570 On behalf of: INTISARI SAINS MEDIS

or

Bank Negara Indonesia (BNI): 1276404081 On behalf of: INTISARI SAINS MEDIS

Notes: *Letter of Acceptance* (LoA) of publication include with Volume, Issues, year of publication, and DOI number of the manuscript will be processed soon after full of payment.



Letter of Acceptance
23 November 2022

**Dear: Nanik Zubaidah¹, Muhammad Luthfi^{2*}, Wisnu Setyari², Retno Palupi³,
Nur Imamatul Ummah⁴, Ardyta Lintang Maheswari⁴, Arif Rahman Nurdianto⁵,
Fathillah Abdul Razak⁶**

¹Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya

²Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya

³Departement of Dental Public Health, Faculty of Dental Medicine, Universitas Airlangga, Surabaya

⁴Undergraduate students, Faculty of Dental Medicine, Universitas Airlangga, Surabaya

⁵Lecture in Universitas Anwar Medika, Sidoarjo, Indonesia

⁶Department of Oral and Craniofacial Sciences. Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

*Corresponding author: m.luthfi@fkg.unair.ac.id

I am very excited to accept your paper entitled:
“Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction.”

Your paper will be published in the issue of of Vol. 11 Number 3, 2022.

<http://dx.doi.org/10.15562/bmj.v11i3.3874>

(Online Link: <http://balimedicaljournal.org/index.php/bmj/article/view/3874>).

And it usually takes 2 to 4 months for your journal to show up at Google Scholar, but if you need it fast, you may add it up manually using your google scholar account. The CrossRef and DOI number usually activate in 3 until 6 months.

Bali Medical Journal is indexed in Web of Sciences, Scopus, and many other indexing organization: <http://balimedicaljournal.org/index.php/bmj/pages/view/indexing>

- | | |
|---|---|
| 1. Web of Science (Clarivate Analytics) | 14. Ulrichsweb.com™ [Proquest] |
| 2. Scopus (Elsevier) | 15. InCites Journal Citation Reports (Web of Science) |
| 3. USA National Library of Medicine (Pubmed) | 16. Harvard Library |
| 4. NIH National Institutes of Health | 17. Index Copernicus |
| 5. HINARI Research in Health | 18. National Library of Australia |
| 6. International Committee of Medical Journal Editors | 19. University of Denmark |
| 7. DOAJ Directory of Open Acces Journals | 20. Library of Science and Technology (China) |
| 8. SINTA-Science and Technology Index | 21. ETH Bibliothek (Switzerland) |
| 9. Portal Garuda | 22. SJIF Journal Rank |
| 10. Google Scholar | 23. Science Impact Factor (SIF) |
| 11. DOI Crossref | 24. Genamics |
| 12. EBSCO Open Science Directory | 25. ASEAN Citation Index (ACI) |
| 13. Sherpa/Romeo | 26. UDL-Edge (Malaysia) |

Please do not hesitate to contact us if you need anything. It has been a pleasure for us to proofread and edit your work, and we are looking forward to your colleagues and your other papers in the near future.

Agreed/Menyetujui by:

Menyetujui,

Bali Medical Journal
Prof. Dr. dr. Sri Maliawan, SpBS (K)
Editor in Chief

Menyetujui,

Bali Medical Journal
Prof. Dr. Ir. Ida Bagus Putra Murtaba, MPhil
Associate Editor

Arif Rahman Nurdianto didins99@gmail.com

Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: nanik-z@fkg.unair.ac.id

----- Forwarded message -----

Dari: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Kam, 10 Nov 2022 13.48

Subject: Re: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: Arif Rahman Nurdianto <didins99@gmail.com>, <m.luthfi@fkg.unair.ac.id>

Dear author,

Regarding your letter for the fee waiver, our chief editor has been given permission to cut off 25% of the APC price. Here we attache the new invoice. Thank you.

Warm regards
Editorial team

On Tue, Nov 8, 2022 at 5:44 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:

----- Forwarded message -----

From: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Mon, Nov 7, 2022, 16:03

Subject: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: <m.luthfi@fkg.unair.ac.id>

Dear Authors,

Thank you for submitting your article entitled: "**Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction**"

Based on our author guidelines, Your article fulfilled the minimum required structure,

<https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidelines>

In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive

(<https://www.balimedicaljournal.org/index.php/bmj/issue/archive>).

According to the new International regulation, please fulfill the requirements below:

1. Ethical clearance number/statement and/or informed consent at the end of the manuscript (**Confirmed**).
2. Please state your conflict of interest in the paper. (**Confirmed**)
3. Please state the funding (if any) in your paper. (**Unconfirmed**)
4. Please state each author's contribution. (**Confirmed**)
5. Numerous grammatical errors were found in the text.

Please fulfill the unconfirmed statement above in the manuscript. Your article has been accepted to publish in our journal with minor revision. The article also has been processed by our editing partner REVISE as per instruction from our executive editor. Therefore, please complete the payment of the APC and the associated fee, so we can proceed to publish your article (Invoice attached). Your LoA will be sent as soon as we confirm your payment and please send us your proof of payment.

Best regards,
Editorial Team BaliMedJ

--

Bali Medical Journal (BaliMedJ)
P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)



Bali Medical Journal Worthy of Publication

Managing Editor:

editor@balimedicaljournal.org

editorbalimedicaljournal@gmail.com

<http://balimedicaljournal.org>

Invoice no: 3874/BMJ/14102022

Invoice date: **November 2022**

Recent Status: **Unpaid**

Valid until: November 10th 2022

Bill to: Muhammad Luthfi (m.luthfi@fkg.unair.ac.id)

Description	Quantity	Price	Amount
Basic Administration and Article Processing Charge (APC): "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 750	USD 750
Proofread and reviewing of Manuscript entitled: "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 100	USD 100
Subtotal			USD 850
Total (Tax 0.5%)			USD 854.25

*Note: please kindly adopt USD exchange to IDR day per day at the mean time you pay the respective APC.

All of the payment can be transferred to Indonesian Bank Account:

Jenius (BTPN): Sintisarisains

or

Bank Syariah Indonesia (BSI): 7099787570 On behalf of: **INTISARI SAINS MEDIS**

or

Bank Negara Indonesia (BNI): 1276404081 On behalf of: **INTISARI SAINS MEDIS**

Notes: *Letter of Acceptance* (LoA) of publication include with Volume, Issues, year of publication, and DOI number of the manuscript will be processed soon after full of payment.

Arif Rahman Nurdianto didins99@gmail.com

Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: nanik-z@fkg.unair.ac.id

----- Forwarded message -----

Dari: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>
Date: Rab, 23 Nov 2022 21.06
Subject: Re: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: Arif Rahman Nurdianto <didins99@gmail.com>

Dear author,

Thank you, we have received the publication payment. Here we attached below the payment proof. Your manuscript will process for the next step. Thank you.

Warm regards
Editorial team

On Thu, Nov 10, 2022 at 6:18 PM Arif Rahman Nurdianto <didins99@gmail.com> wrote:
Thank you very much 🙏

Pada tanggal Kam, 10 Nov 2022 13.48, Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> menulis:
Dear author,

Regarding your letter for the fee waiver, our chief editor has been given permission to cut off 25% of the APC price. Here we attache the new invoice. Thank you.

Warm regards
Editorial team

On Tue, Nov 8, 2022 at 5:44 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:

----- Forwarded message -----

From: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>
Date: Mon, Nov 7, 2022, 16:03
Subject: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: <m.luthfi@fkg.unair.ac.id>

Dear Authors,

Thank you for submitting your article entitled: "**Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction**"

Based on our author guidelines, Your article fulfilled the minimum required structure, <https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidelines>
In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive (<https://www.balimedicaljournal.org/index.php/bmj/issue/archive>).

According to the new International regulation, please fulfill the requirements below:

1. Ethical clearance number/statement and/or informed consent at the end of the manuscript (**Confirmed**).
2. Please state your conflict of interest in the paper. (**Confirmed**)

3. Please state the funding (if any) in your paper. (**Unconfirmed**)
4. Please state each author's contribution. (**Confirmed**)
5. Numerous grammatical errors were found in the text.

Please fulfill the unconfirmed statement above in the manuscript. Your article has been accepted to publish in our journal with minor revision. The article also has been processed by our editing partner REVISE as per instruction from our executive editor. Therefore, please complete the payment of the APC and the associated fee, so we can proceed to publish your article (Invoice attached). Your LoA will be sent as soon as we confirm your payment and please send us your proof of payment.

Best regards,
Editorial Team BaliMedJ

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)



Bali Medical Journal Worthy of Publication

Managing Editor:

editor@balimedicaljournal.org

editorbalimedicaljournal@gmail.com

<http://balimedicaljournal.org>

Invoice no: 3874/BMJ/14102022

Invoice date: **November 2022**

Recent Status: **Paid**

Valid until: November 10th 2022

Bill to: Muhammad Luthfi (m.luthfi@fkg.unair.ac.id)

Description	Quantity	Price	Amount
Basic Administration and Article Processing Charge (APC): "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 750	USD 750
Proofread and reviewing of Manuscript entitled: "Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction"	1	USD 100	USD 100
Subtotal			USD 850
Total (Tax 0.5%)			USD 854.25

*Note: please kindly adopt USD exchange to IDR day per day at the mean time you pay the respective APC.

All of the payment can be transferred to Indonesian Bank Account:

Jenius (BTPN): Sintisarisains

or

Bank Syariah Indonesia (BSI): 7099787570 On behalf of: **INTISARI SAINS MEDIS**

or

Bank Negara Indonesia (BNI): 1276404081 On behalf of: **INTISARI SAINS MEDIS**

Notes: *Letter of Acceptance* (LoA) of publication include with Volume, Issues, year of publication, and DOI number of the manuscript will be processed soon after full of payment.

Arif Rahman Nurdianto didins99@gmail.com

Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: nanik-z@fkg.unair.ac.id

----- Forwarded message -----

Dari: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>
Date: Rab, 23 Nov 2022 21.08
Subject: Re: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: Arif Rahman Nurdianto <didins99@gmail.com>

Automatic Reply: Letter of Acceptance

This email and any attachments are confidential and may also be privileged. If you are not the intended recipient, please delete all copies and notify the sender immediately.

On Wed, Nov 23, 2022 at 10:06 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:
Dear author,

Thank you, we have received the publication payment. Here we attached below the payment proof. Your manuscript will process for the next step. Thank you.

Warm regards
Editorial team

On Thu, Nov 10, 2022 at 6:18 PM Arif Rahman Nurdianto <didins99@gmail.com> wrote:
Thank you very much 🙏

Pada tanggal Kam, 10 Nov 2022 13.48, Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> menulis:
Dear author,

Regarding your letter for the fee waiver, our chief editor has been given permission to cut off 25% of the APC price. Here we attache the new invoice. Thank you.

Warm regards
Editorial team

On Tue, Nov 8, 2022 at 5:44 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:

----- Forwarded message -----

From: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>
Date: Mon, Nov 7, 2022, 16:03
Subject: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]
To: <m.luthfi@fkg.unair.ac.id>

Dear Authors,

Thank you for submitting your article entitled: "**Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction**"

Based on our author guidelines, Your article fulfilled the minimum required structure,

<https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidelines>

In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive (<https://www.balimedicaljournal.org/index.php/bmj/issue/archive>).

According to the new International regulation, please fulfill the requirements below:

1. Ethical clearance number/statement and/or informed consent at the end of the manuscript (**Confirmed**).
2. Please state your conflict of interest in the paper. (**Confirmed**)
3. Please state the funding (if any) in your paper. (**Unconfirmed**)
4. Please state each author's contribution. (**Confirmed**)
5. Numerous grammatical errors were found in the text.

Please fulfill the unconfirmed statement above in the manuscript. Your article has been accepted to publish in our journal with minor revision. The article also has been processed by our editing partner REVISE as per instruction from our executive editor. Therefore, please complete the payment of the APC and the associated fee, so we can proceed to publish your article (Invoice attached). Your LoA will be sent as soon as we confirm your payment and please send us your proof of payment.

Best regards,
Editorial Team BaliMedJ

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

Arif Rahman Nurdianto didins99@gmail.com

Fwd: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: nanik-z@fkg.unair.ac.id

----- Forwarded message -----

Dari: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Jum, 25 Nov 2022 21.35

Subject: Re: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: Arif Rahman Nurdianto <didins99@gmail.com>

Dear Authors,

Attached are the plagiarism report (23%) and the commentary file of your submitted article: Regenerative alveolar bone in dental sockets of diabetic Wistar rats post tooth extraction. The commentary file is a summary of the reviews of your manuscript. Our reviewer suggested several revisions; therefore, several necessary changes will be made. Our editor has fixed all sections in your manuscript according to the reviewer's suggestion. We gladly said that the final manuscript was appropriate for publication and is attached below. We hope you check again your final manuscript before we continue the galley approval process. Please let us know if you agree to publish your final manuscript. Please send the manuscript back to us immediately if you have any fixation. Thank you for your cooperation and for trusting us with your hard work.

Warm Regards,
Editorial Board Member

On Wed, Nov 23, 2022 at 10:08 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:
Automatic Reply: Letter of Acceptance

This email and any attachments are confidential and may also be privileged. If you are not the intended recipient, please delete all copies and notify the sender immediately.

On Wed, Nov 23, 2022 at 10:06 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:
Dear author,

Thank you, we have received the publication payment. Here we attached below the payment proof. Your manuscript will process for the next step. Thank you.

Warm regards
Editorial team

On Thu, Nov 10, 2022 at 6:18 PM Arif Rahman Nurdianto <didins99@gmail.com> wrote:
Thank you very much 🙏

Pada tanggal Kam, 10 Nov 2022 13.48, Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> menulis:
Dear author,

Regarding your letter for the fee waiver, our chief editor has been given permission to cut off 25% of the APC price. Here we attache the new invoice. Thank you.

Warm regards
Editorial team

On Tue, Nov 8, 2022 at 5:44 PM Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> wrote:

----- Forwarded message -----

From: **Editor Bali Medical Journal** <editorbalimedicaljournal@gmail.com>

Date: Mon, Nov 7, 2022, 16:03

Subject: Accepted with Minor Revision [BaliMedJ] [Manuscript ID: 3874]

To: <m.luthfi@fkg.unair.ac.id>

Dear Authors,

Thank you for submitting your article entitled: "**Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction**"

Based on our author guidelines, Your article fulfilled the minimum required structure,

<https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidelines>

In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive

(<https://www.balimedicaljournal.org/index.php/bmj/issue/archive>).

According to the new International regulation, please fulfill the requirements below:

1. Ethical clearance number/statement and/or informed consent at the end of the manuscript (**Confirmed**).
2. Please state your conflict of interest in the paper. (**Confirmed**)
3. Please state the funding (if any) in your paper. (**Unconfirmed**)
4. Please state each author's contribution. (**Confirmed**)
5. Numerous grammatical errors were found in the text.

Please fulfill the unconfirmed statement above in the manuscript. Your article has been accepted to publish in our journal with minor revision. The article also has been processed by our editing partner REVISE as per instruction from our executive editor. Therefore, please complete the payment of the APC and the associated fee, so we can proceed to publish your article (Invoice attached). Your LoA will be sent as soon as we confirm your payment and please send us your proof of payment.

Best regards,
Editorial Team BaliMedJ

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)

--

Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)
[SCOPUS Elsevier](#)
[All Indexing Organisation](#)



--
Bali Medical Journal (BaliMedJ)
P-ISSN: 2089-1180
E-ISSN 2302-2914
Indexed at:
[Web of Science \(WOS\) Clarivate Analytics](#)
[SCOPUS Elsevier](#)
[All Indexing Organisation](#)



--
Bali Medical Journal (BaliMedJ)
P-ISSN: 2089-1180
E-ISSN 2302-2914
Indexed at:
[Web of Science \(WOS\) Clarivate Analytics](#)
[SCOPUS Elsevier](#)
[All Indexing Organisation](#)



--
Bali Medical Journal (BaliMedJ)

P-ISSN: 2089-1180

E-ISSN 2302-2914

Indexed at:

[Web of Science \(WOS\) Clarivate Analytics](#)

[SCOPUS Elsevier](#)

[All Indexing Organisation](#)



Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction

ORIGINALITY REPORT

23%

SIMILARITY INDEX

17%

INTERNET SOURCES

15%

PUBLICATIONS

9%

STUDENT PAPERS

PRIMARY SOURCES

1	www.pubfacts.com Internet Source	2%
2	Submitted to University of Wales Institute, Cardiff Student Paper	2%
3	sciencescholar.us Internet Source	2%
4	Seng - Feng Jeng, Jian - An Chen, Li - Ren Chang, Chien - Chung Chen et al. "Beneficial Effect of Intense Pulsed Light on the Wound Healing in Diabetic Rats", Lasers in Surgery and Medicine, 2019 Publication	1%
5	hithaldia.ac.in Internet Source	1%
6	www.jidmr.com Internet Source	1%
7	"Obesity and Diabetes", Springer Science and Business Media LLC, 2020	1%

-
- 8 Submitted to Tikrit University 1 %
Student Paper
-
- 9 Muhammad Luthfi, Aqsa Sjuhada Oki, Retno Indrawati, Muhaimin Rifai, Yoes Prijatna Dachlan, Fathilah Abdul Razak. "CD89/CD35 Expression Ratio in Salivary Neutrophil as an Early Detection Marker for Severe Early Childhood Caries", European Journal of Dentistry, 2020 1 %
Publication
-
- 10 Agung Sosiawan, Dian Agustin Wahjuningrum, Dini Setyowati, Michelle Suhartono et al. "The relationship between parents' oral hygiene knowledge and children with Down Syndrome's oral hygiene via OHI-S", F1000Research, 2022 1 %
Publication
-
- 11 www.frontiersin.org 1 %
Internet Source
-
- 12 Hammad Ullah, Anna De Filippis, Cristina Santarcangelo, Maria Daglia. "Epigenetic regulation by polyphenols in diabetes and related complications", Mediterranean Journal of Nutrition and Metabolism, 2020 1 %
Publication
-
- 13 www.intechopen.com
Internet Source

		1 %
14	www.endocrino.org.br Internet Source	1 %
15	www.pubmedcentral.nih.gov Internet Source	1 %
16	Submitted to TAFE Queensland Brisbane Student Paper	1 %
17	downloads.hindawi.com Internet Source	1 %
18	Submitted to Universitas Airlangga Student Paper	1 %
19	www.dovepress.com Internet Source	1 %
20	www.drjjournal.net Internet Source	1 %
21	Shahla Korani, Khodabakhsh Rashidi, Mona Hamelian, Ali R. Jalalvand et al. "Evaluation of Antimicrobial and Wound Healing Effects of Gold Nanoparticles Containing Abelmoschus esculentus (L.) Aqueous Extract", Bioinorganic Chemistry and Applications, 2021 Publication	1 %
22	"Abstracts of the EASD, Stockholm 2010", Diabetologia, 2010 Publication	1 %

23 J. Leppiniemi, V.P. Hytönen. "Therapeutic proteins in bioactive materials for wound healing", Elsevier BV, 2017 1 %
Publication

24 hdl.handle.net 1 %
Internet Source

25 www.thieme-connect.de 1 %
Internet Source

Exclude quotes Off

Exclude matches < 1%

Exclude bibliography On

Commentary

Dear Sir/Madam,

Here are some commentaries to the manuscript entitled “Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction”.

No.	Section	Commentary
A	Title and Affiliation	1. Please write the title in Sentence case format. → BMJ editor has revised this part.
B	Abstract	1. The abstract was clear, so there was no revision in this part.
C	Introduction	1. The introduction narration is clear and appropriate. It also contains the study objective; however, the text has numerous grammatical errors. Please improve these conditions. → BMJ editor has revised this part.
D	Method	1. Overall, the method is clear and detailed. It has explained well the procedure of the study; however, there are numerous grammatical errors in the text. Please improve these conditions. → BMJ editor has revised this part.
E	Result	1. The result is well-written and concise. The data are also well presented in the table. There is no revision in this section. → BMJ editor has revised this part.
F	Discussion	1. The discussion is well-written. It has compared the result with others and related to basic theory. The limitations of the study have also been described in the text. Please improve the grammatical writing due to numerous errors found in the text. → BMJ editor has revised this part.
G	Conclusions	1. The narration has well concluded the study
H	Table, figure and Reference	1. Please write the citations and the references in Vancouver style format. → BMJ editor has revised this part.
I	Others	1. Please complete the checklist attached on the <i>next page</i> .

JBI CRITICAL APPRAISAL CHECKLIST FOR QUASI-EXPERIMENTAL STUDIES

Reviewer BMJ Reviewer Date November 15th

Author Nanik Zubaidah Year 2022 Record Number _____

	Yes	No	Unclear	Not applicable
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the participants included in any comparisons similar?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Was there a control group?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of participants included in any comparisons measured in the same way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Comments (Including reason for exclusion)

Appropriate to publish

ORIGINAL RESEARCH

Regenerative Alveolar Bone in Dental Sockets

Zubaidah et al

Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction

Nanik Zubaidah¹

Muhammad Luthfi²

Wisnu Setyari²

Retno Palupi³

Nur Imamatul Ummah⁴

Ardyta Lintang Maheswari⁴

Arif Rahman Nurdianto⁵

Fathillah Abdul Razak⁶

¹Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya;

²Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya; ³Departement of

Dental Public Health, Faculty of Dental Medicine, Universitas Airlangga, Surabaya; ⁴Undergraduate students,

Faculty of Dental Medicine, Universitas Airlangga, Surabaya; ⁵Lecture in Universitas Anwar Medika, Sidoarjo,

Indonesia; ⁶Department of Oral and Craniofacial Sciences. Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

Correspondence: Muhammad Luthfi

Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya

Email: m.luthfi@fkg.unair.ac.id

Abstract:

Background: The bone healing of the alveolar socket post-dental extraction is critical in dental services. Delayed healing is a common problem in diabetes mellitus (DM) patients. It is due to the impaired angiogenic response and microvascular complications. Okra fruit extract can control diabetes mellitus (DM) in several ways, delaying glucose absorption and regenerating pancreatic cells. It can impact an increase in insulin secretion and glycogenesis to control hyperglycemia in DM. This study analyzed the regenerative alveolar bone through the expression of TGF- β 2 in the tooth socket of Wistar rats with diabetes mellitus post-extraction after administration of okra fruit extract.

Patients and methods: Extraction of the rat mandibular left incisor was performed using a pair of modified forceps. The tooth sockets were then rinsed using a saline solution. Two groups (control & treatment) of four rats were sacrificed on days 3, 5, and 7. The socket tissues from the rats were then immunohistochemically analyzed

Results: The average level of TGF- β 1 expression in the treatment (T) groups was higher compared to the control (C) group: day 3 (10.50 \pm 2.67 versus 4.83 \pm 1.17), day 5 (12.33 \pm 1.63 versus 5.17 \pm 2.32), and day 7 (13.00 \pm 2.83 versus 4.50 \pm 1.05), with P = 0.000

Conclusion: The administration of okra fruit extract can increase regenerative alveolar bone healing through increased expression of TGF- β 2 in the dental socket after tooth extraction of diabetic Wistar rats.

Keywords: Diabetes mellitus, okra fruit, TGF- β 2, wound healing, bone regenerative

Introduction

Bone tissue regeneration is an important problem in medicine and dentistry, one of which is abnormalities due to infectious diseases. One of the goals of treating bone defects is to restore the normal morphology and function of the damaged structures. The process of bone formation goes through two phases, namely endochondral ossification and intramembrane ossification.¹ An excellent balance between osteoblasts and osteoclasts are the two primary bone cells involved in the process of bone remodeling. Osteoblasts are responsible for bone formation, while osteoclasts are bone-absorbing cells.²

Wound healing is a dynamic process that completely restores anatomic integrity with other functions without spreading infection. Acute wounds generally heal quickly without causing problems if there are no disturbances in physiological functions such as poor blood circulation, obesity, diseases such as diabetes, and stress. Chronic wounds are tissue wounds that do not heal in an organized series of stages and take more than 12 weeks to heal.^{3,4} In general, the healing process begins with hemostasis due to blood loss and microbial invasion of the wound area. This phase is followed rapidly and overlaps with the inflammatory phase, which initially begins with the infiltration of proinflammatory neutrophil cells, followed by macrophages, the release of growth factors and cytokines, and other cells. The proliferative phase overlaps with the inflammatory phase. It includes new tissue and blood vessels (angiogenesis), and matrix construction is initiated to fill the injured area. The final remodeling phase then increases the tensile strength of the extracellular matrix and reduces blood supply to the damaged area.⁵

Diabetes mellitus (DM) can disrupt various wound-healing processes. It includes hemostasis, inflammation, proliferation, and remodeling phases. This problem will impact long-term adverse effects on quality of life, morbidity, and mortality characterized by chronic wounds that cause impaired healing due to delayed or uncoordinated healing. DM shows a persistent inflammatory phase due to obstacles in forming granulation tissue and reduced wound tensile strength caused by damage to blood vessels that cause ischemia.⁶

Diabetic disease can delay the healing process leading to non-healing wounds. Some various complications are identified, such as functional impairment and infections. The common infections in diabetic patients are cellulitis, abscesses, osteomyelitis, gangrene, and septicemia. The wound-healing process requires collaboration between inflammatory cells and biochemical mediators stimulated by various factors. Changes in cellular and biochemical factors and their activities have been implicated in the failure of wound healing in diabetics. The cells involved in wound healing are neutrophils, monocytes, macrophages, keratinocytes, fibroblasts, T cells, B cells, mast cells, and endothelial cells. These cells actively produce and regulate various cytokines and growth factors. Monocytes, which then turn into macrophages, produce proinflammatory cytokines IL-1 β , TNF-, IL-6, and VEGF5 IGF-1. TGF- β is the main factor in both diabetic and non-diabetic conditions. Neutrophils and T and B cells are also significant producers of TNF-, IL-10, and other cells,

keratinocytes, fibroblasts, mast cells, and endothelial cells. These cells also contribute to the production of VEGF, IGF-1, and TGF- β .⁷

Studies reveal that in diabetes, a complex mechanism involving the molecular level is responsible for delayed wound healing. Activities include sustained production of proinflammatory cytokines, impaired angiogenic response, and microvascular complications.⁶ It also impaired macrophage and neutrophil function,⁸ migration and proliferation of keratinocytes, fibroblasts, and impaired factor production. Cure-related disorders such as impaired growth factor production have been reported in animal models of diabetes.⁹ Macrophages are essential contributors to healing. Hyperglycemia and oxidative stress alter the epigenetic code, resulting in macrophage polarization and modulation changes. Dysregulated macrophage polarization is one of the main reasons for delayed wound healing.^{10,11}

Okra fruit contains chemicals such as saponins, tannins, alkaloids, and flavonoids. In addition, okra has quercetin which functions as an antioxidant and antitumor. Its antioxidant properties inhibit endothelial cell migration.¹² Saponins are another active substance in okra, which have antibacterial activity and stimulate angiogenesis. Furthermore, it was shown that flavonoids, mediators of type III collagen synthesis, act as anti-inflammatory agents, modulate oxidative burst in neutrophils, and act as phospholipase inhibitors.¹³ Flavonoids also reduce reactive oxygen species (ROS). Therefore, it can potentiate wound healing.¹⁴

This study aims to analyze the expression of growth factor TGF- β 1 in post-extraction tooth sockets in diabetic Wistar rats.

Material and methods

Research Design and Animal Model

This study is a laboratory-based of experimental analytic study. Wistar rats used as samples in this study were obtained from the Experimental Animal Unit of the Biochemical Laboratory of the Faculty of Medicine, Universitas Airlangga. Research Ethical Committee Faculty of Dental Medicine Universitas Airlangga approved the study (No. 561/HRECC.FODM/X/2021).

Collection, adjustment, maintenance, and treatment were carried out in the Experimental Animal Unit of the Biochemical Laboratory of the Faculty of Medicine, Universitas Airlangga. Okra fruit was extracted in Materia

Medika Batu, Malang, East Java. Histological preparations were carried out at the Anatomy Pathology Laboratory of the Faculty of Medicine, Universitas Airlangga.

Immunohistochemistry staining was used to examine the TGF- β 2 expressed cell. The examination was conducted at the Laboratory of Biochemistry, Faculty of Medicine, Universitas Brawijaya, Malang.

Okra fruit extract preparation

Fresh okra fruit was dried in a drying oven until a constant weight was reached. The dried fruit was then ground into powder. A total of 2 grams of powder was extracted with 20 ml of 70% ethanol in a ratio of 1:10 (w/v) during the maceration period (24 hours) at room temperature. The solvent and soaked powder mixture was filtered through filter paper and then concentrated to 1 ml with a rotary evaporator and diluted with 5% dimethyl sulfoxide (DMSO) at a ratio of 1:1 (v/v). The results were stored at a temperature of minus 20 OC until further use.^{15,16}

Research Procedure

In this study, 24 male Wistar rats aged 2-3 months with a weight of 150-200 grams were adapted in the same cage at 25 ± 2 °C. The 24 Wistar rats were divided into two groups (control group and treatment group). The rats were supplied with standard pellet food and distilled water ad libitum for seven days and 4 hours before being induced with streptozotocin (STZ) (Nacalai Tesque Inc., Japan). The 2% STZ solution was dissolved with 0.1 mol/L citrate buffer solution pH 4.4 at a 45 mg/kg dose and converted to a dose of 6.75 mg/150gr. The solution was then administered to the Wistar rats through intraperitoneal induction. Blood glucose levels were measured on day three after STZ induction by taking a blood sample from the lateral veins in the rats' tails. Measurements were performed using a glucometer (Accu Chek® Instant). The Wistar rats were diagnosed with DM if the blood glucose levels were ≥ 200 mg/dl after the STZ induction (Qinna and Badwan, 2015).¹⁷

Wistar rats with DM were then anesthetized through peritoneal injection using 0.1 ml of ketamine per rat. After the injection, a resting period of 1-1.5 hours was given, after which extractions of the rats' mandibular left incisors were performed using a pair of modified forceps and an elevator. The tooth sockets were then irrigated with saline solution.¹⁸

In the control group, the animals did not receive the administration of okra fruit extract.

Instead, they were only supplied with distilled water prior to the observation. KO1 was observed on the third day, KO2 was observed on the 5th day, and KO3 was observed on the seventh day. In the treatment group, the rats were given oral administration of okra fruit extract after the tooth extraction with a dose of 250 mg/kg, which was converted to a dose of 37.5 mg/150 gr once a day. PO1 was observed on the third day, PO2 on the fifth day, and PO3 on the seventh day.

Wistar rats were sacrificed on the 3rd, fifth and seventh day using a lethal injection of intraperitoneal ketamine (no less than four times the anesthetic dose or about 0.4 ml/kg). The mandibular of each rat was taken from the temporomandibular joint. After this, the Wistar rats were buried according to the ethical treatments of experimental animals. The mandibles in the incisor area were cut vertically and treated with paraffin.¹⁹ The immunohistochemical examination using the method used by Luthfi et al.²⁰ We count the expressed cell in a Light microscope with 400x magnification. The expressed cell number was evaluated on 4 microscopic fields, and the average of TGF- β 2 expressed cells per microscopic field was analyzed statistically.

Statistical Analysis

Statistical analysis was performed using SPSS (IBM SPSS Statistics for Windows, Version 24.0: IBM Corp., USA). The Shapiro-Wilk test was used to find out normally distributed data. After the distribution test, Levene's homogeneity test was then performed. The data that showed normal distribution was homogeneous, and then analysis was continued with the One Way ANOVA test and multiple comparison tests using Tukey HSD.

Results

The study ended in 7 days of the experiment. There was any Wistar rat that died during the study. The data of the TGF- β 2 expressed cell we collected and tabulated and statistical analyses. Tables 1 and 2 show that all the data are typically distributed based on the Shapiro-Wilk test ($p = 0.124$) and homogeneous based on the Levene test ($p = 0.533$). There is no impact of the interaction between time and treatment against TGF- β 2

cell expression (Table 4; $p > 0.05$). However, shows a significant difference between the control versus treatment groups (Figure 1; Table 5; $p = 0.000$).

The study has been conducted, control versus treatment, to evaluate the effect of okra fruit extract in the healing process of the dental socket post extraction. The blood glucose level of all rats was above 200mg/dl after the induction.

The TGF- β 2 expression appears as gradients of yellow to brown stains (red arrow). Figure 2 shows that on the third day, the PO1 group showed an increasing number of TGF- β 2 expressions compared to the KO1 group. On the fifth day, PO2 showed an increasing number of TGF- β 2 expressions compared to the KO2 group. On the seventh day, PO3 showed an increasing number of TGF- β 2 expressions compared to the KO3 group.

Discussion

Routine wound healing is a well-coordinated and synchronized process by factors. It includes growth factors, matrix metalloproteinases (MMP), cytokines, neutrophil cells, proinflammatory macrophages, keratinocytes, fibroblasts, and endothelial cells. Growth factors are biologically active polypeptides that are involved in all phases of the healing process.²¹ Growth factors occur in the early inflammatory and granulation phases, namely tissue formation. Wound healing disorders are caused by defects in the type and growth factors. This healing disorder is due to changes in expression, decreased production, release, trapping, and excessive degradation.²²

The balance between matrix formation and matrix degradation characterizes ECM synthesis with optimal healing. Factors that regulate ECM formation, such as VEGF, IGF-I, IGF-II, TGF- β , KGF24, PDGF25, EGF26, and FGF27 stated that TNF- and IL-6 markedly decreased in diabetic patients.²³ Growth factors are essential in initiating and maintaining the different phases of wound healing. Any changes i.e., down-regulation of growth factor receptors and rapid degradation of growth factor, cause delayed wound healing in diabetics.

The flavonoid is an antioxidant in okra fruit extract (*Abelmoschus esculentus*). It shows a high reactive hydroxyl group that can react with the reactive component of free radicals so that the formation of ROS can be stable and controlled, characterized by a balance between oxidants and antioxidants.²⁴ Flavonoids also act as anti-

inflammatory agents through immunomodulatory mechanisms. Flavonoids can increase Th-1 and Th-2 production and IFN production, which can induce the formation of M1 and M2. M1 formed can play a role in phagocyte apoptosis from neutrophils. An induced shift from phenotype M1 macrophages to M2 results in growth factors such as VEGF. Anti-inflammatory mechanisms in flavonoids can also reduce the activity of cyclooxygenase, which causes reduced prostaglandin synthesis, so the inflammation process increases.²⁵

The low expression in the control group compared to the treatment group is due to the diabetic state after injection of hyperglycemia, which causes the formation of Advanced Glycation End Products (AGEs). If AGEs bound to the Receptor for Advanced Glycation End Products (RAGE) will increase the activation of Mitogen-Activated Protein Kinases (MAPKs), Phosphatidylinositol-3 Kinases (P13-K), and Nicotinamide Adenine Dinucleotide Phosphate Oxidase (NOX) which are the primary sources of the formation of ROS (Luevano-Contreras et al., 2013; Sanches et al., 2018). This Mechanism can lead to activation (NF- κ B) which transcribes proinflammatory cytokines such as TNF- α , IL-6, and IL-1 β . In diabetic Wistar rats with chronic lesions, the ability of macrophages to neutralize neutrophils decreases so that they cannot induce shifting from M1 to M2. The increase of proinflammatory caused by the activation of NF- κ B and dysregulation of shifting M1 to M2 can cause Wistar diabetic mice to experience a persistent inflammatory phase so that it becomes chronic inflammation.²⁶

Okra fruit contains other substances, such as quercetin, which besides acting as an antioxidant, also has antitumor properties. Antitumor properties of quercetin relate to its ability to prevent tumor vascularization by inhibiting the growth and migration of endothelial cells.²⁷ Okra fruit extract at 30% can promote angiogenesis in post-extracted tooth sockets of Wistar rats.²⁰

The proliferation phase comprises re-epithelization, angiogenesis, granulated tissue formation, and collagen deposition, starting on day four until two weeks after injury. The proliferation phase denotes the earlier-formed matrices formation during the hemostasis. It will be replaced by granulated tissue consisting of fibroblasts, granulocyte, macrophage, and newly-formed capillaries. The migration and proliferation of fibroblast cells constitute a response toward the growth factors, namely platelet derivate growth factor (PDGF), tumor growth factor- β (TGF- β), b fibroblast growth factor (bFGF), which are secreted by platelets and macrophages. Fibroblast will proliferate and secrete proteinase. Such as matrix metalloproteinase (MMP) to degrade the surrounding matrices and replace them with collagen and extracellular matrices (ECM).^{28,29}

In this study, on days 3 and 5, and 7, we observed an increase of TGF- β 2 due to the flavonoids in okra. It can reduce the release of prostaglandins and proinflammatory mediators by inhibiting the cyclooxygenase enzyme.³⁰ In addition, flavonoids can also reduce oxidative stress by regulating the activity of NF- κ B so that the increase in proinflammatory cytokines can be reduced. The decrease causes inducible Nitric Oxide Synthase (iNOS) activity to be suppressed to accelerate the wound-healing process.²⁸

A previous study by Pang et al. found that low-dose flavonoids alone could stimulate the expression of TGF- β growth factor, which increased TGF- β levels until the seventh day and in the wound healing process is a stimulator of fibroblast cells.³¹ Giving okra 30% fruit extract gel in the tooth socket after extraction can increase fibroblast cell proliferation.²⁰

The world has seen a rapid increase in the incidence of diabetes generally, and type 2 diabetes has become the most common metabolic disease globally. The increased diabetic state has been partly due to a growth in obesity. It is especially also due to the excess visceral adiposity. In addition, the associated "metabolic syndrome" encompasses insulin resistance, hyperglycemia, dyslipidemia, and hypertension.³²

Inflammation occurs in response to various pathological stimuli and tissue injury. Chronic inflammation and immune system activation may be mainly responsible for obesity-related metabolic diseases such as type 2 diabetes.^{32,33} Critical characteristics of type 2 diabetes include insulin secretion defects and insulin resistance in the liver, adipose tissue, and skeletal muscles. Diabetes and associated complications result from the inflammatory processes.³⁴

The antidiabetic qualities of quercetin involve the stimulation of glucose uptake through a MAPK insulin-dependent mechanism. Stimulating the Mechanism in skeletal muscles has resulted in glucose transporter 4 (GLUT4) translocation. This role for MAPK is distinct from its role in the liver, where it reduces sugar production mainly through the downregulation of vital gluconeogenesis enzymes (Haddad et al., 2015).³⁵

Studies have been conducted on the effects of quercetin in animals with type 2 diabetes.³⁶ Those who received quercetin showed lower glucose plasma levels than the control group and did not experience an increase or decrease in insulin measured by the homeostasis model. Animals that received a 0.08% portion of quercetin showed various other improvements. It includes an increase in plasma adiponectin HDL-cholesterol, decreases in plasma total cholesterol and triacylglycerols, and increases in specific liver enzyme activities important in detoxification. Quercetin is pivotal in improving renal function in diabetic nephropathic rats by

blocking the overexpression of connective tissue growth factor (CTGF) and transforming growth factor- β 1 (TGF- β 1). End-stage renal disease is closely associated with diabetic nephropathy. Studies show that TGF- β 1 and CTGF have an essential impact on the DN pathophysiological systems. Studies examined the impact of quercetin on TGF- β 1, and CTGF renal functions in streptozotocin (STZ) induced diabetic Sprague-Dawley rats.³⁷ Results showed that rats treated with quercetin reduced their kidney and body weight ratio. The expressions of CTGF and TGF- β 1 are higher in the renal tissues. For those that received quercetin, the overexpression was decreased.

Finally, quercetin has been shown to produce an effective in vitro block against lens aldose reductase and prevent polyol accumulation.³⁸ For humans, quercetin has been shown to help decrease the seriousness of numbness, jolting pain, and irritation for patients with type 2 diabetes neuropathy. It has further shown that active quercetin treatment can improve various quality-of-life matrices.³⁹

Conclusion

Administration of okra fruit extract increased the expression of TGF- β 2, which indirectly increased alveolar socket bone healing in the context of regenerative dentistry.

Acknowledgments

We thank to Mr. Heri for supporting us during the animal experiment in the laboratory of Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya.

Disclosure

There is not any conflict of interest.

Author Contribution

All author contributed in the research.

References

1. Soltanoff CS, Yang S, Chen W, Li Y-P. Signaling networks that control the lineage commitment and differentiation of bone cells. *Crit Rev Eukaryot Gene Expr.* 2009;19(1):1–46. Available from: <https://pubmed.ncbi.nlm.nih.gov/19191755>
2. Huang W, Yang S, Shao J, Li Y-P. Signaling and transcriptional regulation in osteoblast commitment and differentiation. *Front Biosci.* 2007;12:3068–92. Available from: <https://pubmed.ncbi.nlm.nih.gov/17485283>
3. Mohandas A, Anisha BS, Chennazhi KP, Jayakumar R. Chitosan–hyaluronic acid/VEGF loaded fibrin nanoparticles composite sponges for enhancing angiogenesis in wounds. *Colloids Surfaces B Biointerfaces.* 2015;127:105–13. Available from: <http://dx.doi.org/10.1016/j.colsurfb.2015.01.024>
4. Anisha BS, Biswas R, Chennazhi KP, Jayakumar R. Chitosan–hyaluronic acid/nano silver composite sponges for drug resistant bacteria infected diabetic wounds. *Int J Biol Macromol.* 2013;62:310–20. Available from: <http://dx.doi.org/10.1016/j.ijbiomac.2013.09.011>
5. Singh MR, Saraf S, Vyas A, Jain V, Singh D. Innovative approaches in wound healing: trajectory and advances. *Artif Cells, Nanomedicine, Biotechnol.* 2013;41(3):202–12. Available from: <http://dx.doi.org/10.3109/21691401.2012.716065>
6. Alavi A, Sibbald RG, Mayer D, Goodman L, Botros M, Armstrong DG, et al. Diabetic foot ulcers. *J Am Acad Dermatol.* 2014;70(1):1.e1-1.e18. Available from: <http://dx.doi.org/10.1016/j.jaad.2013.06.055>
7. Babaei S, Bayat M, Nouruzian M, Bayat M. Pentoxifylline improves cutaneous wound healing in streptozotocin-induced diabetic rats. *Eur J Pharmacol.* 2013;700(1–3):165–72. Available from: <http://dx.doi.org/10.1016/j.ejphar.2012.11.024>
8. Okizaki S, Ito Y, Hosono K, Oba K, Ohkubo H, Amano H, et al. Suppressed recruitment of alternatively activated macrophages reduces TGF- β 1 and impairs wound healing in streptozotocin-induced diabetic mice. *Biomed & Pharmacother.* 2015;70:317–25. Available from: <http://dx.doi.org/10.1016/j.biopha.2014.10.020>
9. Loots MAM, Kenter SB, Au FL, van Galen WJM, Middelkoop E, Bos JD, et al. Fibroblasts derived from chronic diabetic ulcers differ in their response to stimulation with EGF, IGF-I, bFGF and PDGF-AB compared to controls. *Eur J Cell Biol.* 2002;81(3):153–60. Available from: <http://dx.doi.org/10.1078/0171-9335-00228>
10. Basu Mallik S, Jayashree BS, Shenoy RR. Epigenetic modulation of macrophage polarization-perspectives in diabetic wounds. *J Diabetes Complications.* 2018;32(5):524–30. Available from: <http://dx.doi.org/10.1016/j.jdiacomp.2018.01.015>
11. Maruyama K, Asai J, Li M, Thorne T, Losordo DW, D'Amore PA. Decreased macrophage number and activation lead to reduced lymphatic vessel formation and contribute to impaired diabetic wound healing. *Am J Pathol.* 2007;170(4):1178–91. Available from: <https://pubmed.ncbi.nlm.nih.gov/17392158>

12. Alhaji Isa M. THE INVITRO ANTIBACTERIAL ACTIVITY OF OKRA (*Abelmoschus esculentus*) AGAINST SOME SELECTED BACTERIA FROM MAIDUGURI, NORTH EASTERN NIGERIA. 2015;2.
13. D SK, T ET, K AK, A PK, D BSR, Nadendla R. A REVIEW ON: ABELMOSCHUS ESCULENTUS (OKRA). *Int Res J Pharm Appl Sci*. 2013;3(4 SE-Review Articles):129–32. Available from: <https://scienztech.org/index.php/irjpas/article/view/586>
14. Soemarie Y. UJI AKTIVITAS ANTIINFLAMASI KUERSETIN KULIT BAWANG MERAH (*Allium cepa* L.) PADA MENCIT PUTIH JANTAN (*Mus musculus*). *J Ilm Ibnu Sina*. 2016;1(2 SE-Artikel). Available from: <https://e-jurnal.stikes-isfi.ac.id/index.php/JIIS/article/view/46>
15. Yeo YL, Chia YY, Lee CH, Sheng Sow H, Sum Yap W. Effectiveness of Maceration Periods with Different Extraction Solvents on in-vitro Antimicrobial Activity from Fruit of *Momordica charantia* L. *J Appl Pharm Sci*. 2014;4(10):16–23. Available from: <http://dx.doi.org/10.7324/japs.2014.401004>
16. Luthfi M, Juliastuti WS, Asyhari NPO. The Effect Of Giving Okra (*Abelmoschus Esculentus*) Extract On The Increase Of Vascular Endothelial Growth Factor (Vegf). *Indones J Dent Med*. 2019;2(2):35. Available from: <http://dx.doi.org/10.20473/ijdm.v2i2.2019.35-40>
17. Qinna NA, Badwan AA. Impact of streptozotocin on altering normal glucose homeostasis during insulin testing in diabetic rats compared to normoglycemic rats. *Drug Des Devel Ther*. 2015;9:2515–25. Available from: <https://pubmed.ncbi.nlm.nih.gov/26005328>
18. Gunawan F, Sularsih, Seomartono. Perbedaan Kitosan Berat Molekul Rendah dan Tinggi Terhadap Jumlah Sel Limfosit pada Proses Penyembuhan Luka Pencabutan Gigi. *DENTA*. 2021;9(1):113–21. Available from: <https://journal-denta.hangtuah.ac.id/index.php/jurnal/article/view/213>
19. El Hady T, Karam S, El Sawa A, Saad N. EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR DURING HEALING OF EXTRACTION SOCKETS IN DIABETIC RATS. *Alexandria Dent J*. 2015;40(1):120–5. Available from: <http://dx.doi.org/10.21608/adjalexu.2015.58746>
20. Luthfi M, Juliastuti WS, Risky YA, Wijayanti EH, Rachmawati AE, Asyhari NPO. Expression of fibroblast cells after extraction of wistar rat teeth after topical application of okra fruit (*Abelmoschus esculentus*) gel. *Infect Dis Rep*. 2020;12(Suppl 1):8726. Available from: <https://pubmed.ncbi.nlm.nih.gov/32874458>
21. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. PERSPECTIVE ARTICLE: Growth factors and cytokines in wound healing. *Wound Repair Regen*. 2008;16(5):585–601. Available from: <http://dx.doi.org/10.1111/j.1524-475x.2008.00410.x>
22. Crovetti G, Martinelli G, Issi M, Barone M, Guizzardi M, Campanati B, et al. Platelet gel for healing cutaneous chronic wounds. *Transfus Apher Sci*. 2004;30(2):145–51. Available from: <http://dx.doi.org/10.1016/j.transci.2004.01.004>
23. Patel S, Srivastava S, Singh MR, Singh D. Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing. *Biomed & Pharmacother*. 2019;112:108615. Available from: <http://dx.doi.org/10.1016/j.biopha.2019.108615>

24. Durga M, Nathiya S, Devasena T. Immunomodulatory and antioxidant actions of dietary flavonoids. *Int J Pharm Pharm Sci.* 2014;6:50–6.
25. Landén NX, Li D, Ståhle M. Transition from inflammation to proliferation: a critical step during wound healing. *Cell Mol Life Sci.* 2016/05/14. 2016;73(20):3861–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/27180275>
26. Krzyszczyk P, Schloss R, Palmer A, Berthiaume F. The Role of Macrophages in Acute and Chronic Wound Healing and Interventions to Promote Pro-wound Healing Phenotypes. *Front Physiol.* 2018;9:419. Available from: <https://pubmed.ncbi.nlm.nih.gov/29765329>
27. Xia F, Zhong Y, Li M, Chang Q, Liao Y, Liu X, et al. Antioxidant and Anti-Fatigue Constituents of Okra. *Nutrients.* 2015;7(10):8846–58. Available from: <https://pubmed.ncbi.nlm.nih.gov/26516905>
28. Qing C. The molecular biology in wound healing & non-healing wound. *Chinese J Traumatol = Zhonghua chuang shang za zhi.* 2017/06/30. 2017;20(4):189–93. Available from: <https://pubmed.ncbi.nlm.nih.gov/28712679>
29. Jimenez PA, Jimenez SE. Tissue and cellular approaches to wound repair. *Am J Surg.* 2004;187(5):S56–64. Available from: [http://dx.doi.org/10.1016/s0002-9610\(03\)00305-2](http://dx.doi.org/10.1016/s0002-9610(03)00305-2)
30. Rathee P, Chaudhary H, Rathee S, Rathee D, Kumar V, Kohli K. Mechanism of Action of Flavonoids as Anti-inflammatory Agents: A Review. *Inflamm & Allergy - Drug Targets.* 2009;8(3):229–35. Available from: <http://dx.doi.org/10.2174/187152809788681029>
31. Bao D, Wang J, Pang X, Liu H. Protective Effect of Quercetin against Oxidative Stress-Induced Cytotoxicity in Rat Pheochromocytoma (PC-12) Cells. *Molecules.* 2017;22(7):1122. Available from: <https://pubmed.ncbi.nlm.nih.gov/28684704>
32. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. *Nat Rev Immunol.* 2011;11(2):98–107. Available from: <http://dx.doi.org/10.1038/nri2925>
33. Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. *Nat Rev Immunol.* 2011/01/21. 2011;11(2):85–97. Available from: <https://pubmed.ncbi.nlm.nih.gov/21252989>
34. Zozulinska D, Wierusz-Wysocka B. Type 2 diabetes mellitus as inflammatory disease. *Diabetes Res Clin Pract.* 2006;74(2):S12–6. Available from: <http://dx.doi.org/10.1016/j.diabres.2006.06.007>
35. Eid HM, Nachar A, Thong F, Sweeney G, Haddad PS. The molecular basis of the antidiabetic action of quercetin in cultured skeletal muscle cells and hepatocytes. *Pharmacogn Mag.* 2015;11(41):74–81. Available from: <https://pubmed.ncbi.nlm.nih.gov/25709214>
36. Jeong S-M, Kang M-J, Choi H-N, Kim J-H, Kim J-I. Quercetin ameliorates hyperglycemia and dyslipidemia and improves antioxidant status in type 2 diabetic db/db mice. *Nutr Res Pract.* 2012/06/30. 2012;6(3):201–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/22808343>
37. Lai P-B, Zhang L, Yang L-Y. Quercetin Ameliorates Diabetic Nephropathy by Reducing the Expressions of Transforming Growth Factor- β 1 and Connective Tissue Growth Factor in Streptozotocin-Induced Diabetic Rats. *Ren Fail.* 2011;34(1):83–7. Available from:

<http://dx.doi.org/10.3109/0886022x.2011.623564>

38. Chaudhry PS, Cabrera J, Juliani HR, Varma SD. Inhibition of human lens aldose reductase by flavonoids, sulindac and indomethacin. *Biochem Pharmacol.* 1983;32(13):1995–8. Available from:

[http://dx.doi.org/10.1016/0006-2952\(83\)90417-3](http://dx.doi.org/10.1016/0006-2952(83)90417-3)

39. Valensi P, Le Devehat C, Richard J-L, Farez C, Khodabandehlou T, Rosenbloom RA, et al. A multicenter, double-blind, safety study of QR-333 for the treatment of symptomatic diabetic peripheral neuropathy. *J Diabetes Complications.* 2005;19(5):247–53. Available from:

<http://dx.doi.org/10.1016/j.jdiacomp.2005.05.011>

Table 1. Shapiro test for normality of TGF-β2 expression in control and treatment groups

	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	Df	Sig.
Residual for TGF-β2	.108	36	.200	.952	36	.124

Table 2. Levene test Homogeneity of the data of TGF-β2 expression cell in control and treatment group.

Group	N	Mean ± Standard Deviation	Sig.
KO1	6	4.8333 ± 1.16905	0.533
KO2	6	5.1667 ± 2.31661	
KO3	6	4.5000 ± 1.04881	
PO1	6	10.5000 ± 2.66458	
PO2	6	12.3333 ± 1.63299	
PO3	6	13.0000 ± 2.82843	

Notes::*: KO=Control group; PO=Treatment group; 1,2,3 are day 3, 5 and 7; N = number of Wistar rats per group.

Table 3. Descriptive data of the mean and standard deviation of the treatment and control groups based on days of evaluation

Days Evaluation	N	Group	Mean ± SD
3	6	KO1	4.8333 ± 1.16905
	6	PO1	10.5000 ± 2.66458
5	6	KO2	5.1667 ± 2.31661
	6	PO2	12.3333 ± 1.63299
7	6	KO3	4.5000 ± 1.04881
	6	PO3	13.0000 ± 2.82843

Note: N=the number of rat in each group; KO = Control; PO = Treatment

Table 4. Two way ANOVA test between control and treatment groups and their interactions

Variables	P value	Eta squared
Time	0.346	.068
Group	0.000	.780
Time * Group	0.259	.086

Table 5. Comparative test results of TGF-β2 based on treatment

Group	Mean ± SD	Sig.
Treatment	4,83 ± 1,54	0.000
Control	11,94 ± 2.53	

Figure 1. Graph the average of TGF- β 2 expression cells on days 3, 5, and 7 in the socket tissue of Wistar rats in the control group and the treatment group

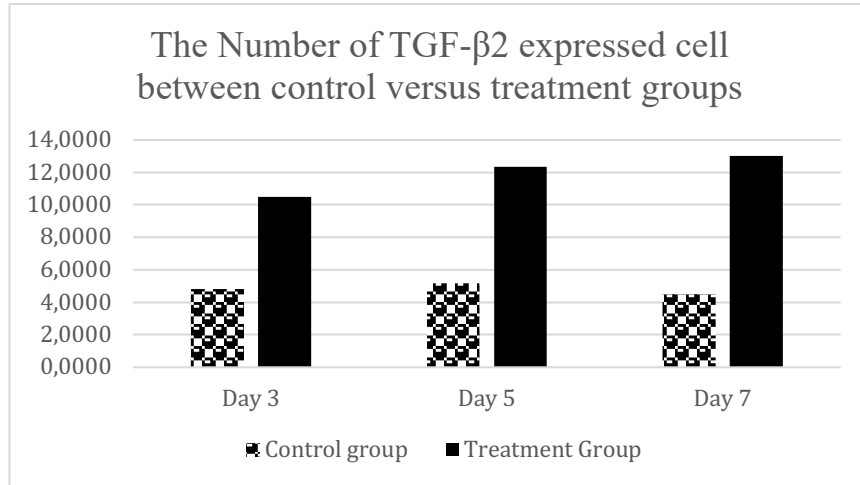
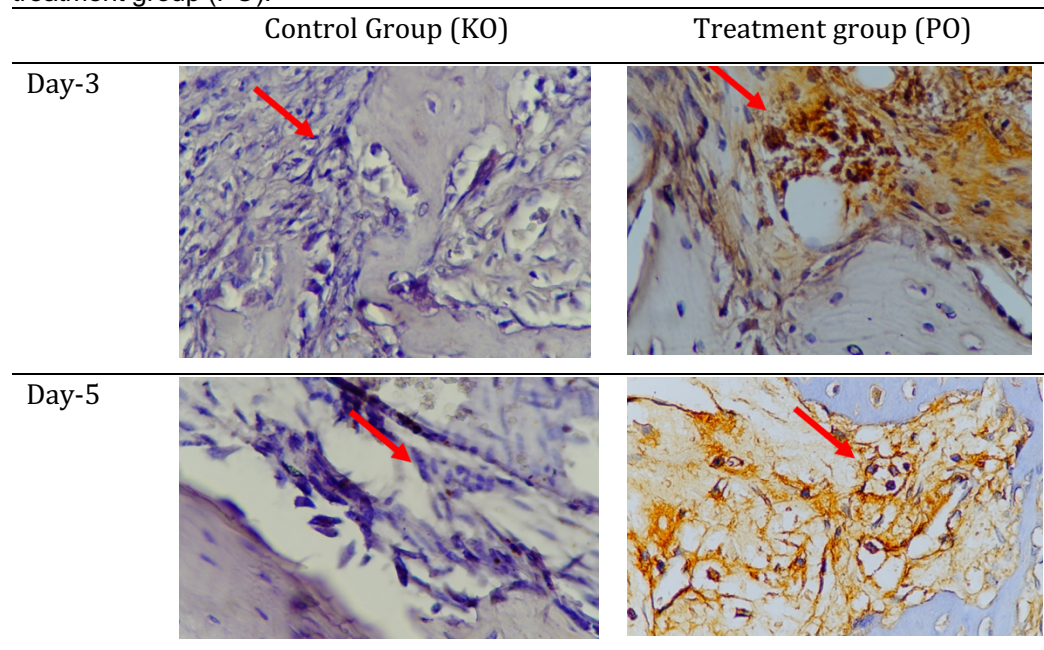


Figure 2. Expression of TGF- β 2 days 3,5 and 7 in the socket tissue of Wistar rats with Diabetes Mellitus on immunohistochemical examination under a 400x magnification microscope in the control group (KO) and the treatment group (PO).



Day-7

