



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**Manuscript NO:** 40147

**Title:** Exercise and glucagon-like peptide-1: Does exercise potentiate the effect of treatment?

**Reviewer’s code:** 02631746

**Reviewer’s country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-06-04

**Date reviewed:** 2018-06-04

**Review time:** 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Well organised manuscript showing possible relationship between exercise and GLP-1 and its impact on DM. THE hypothesis is reasonable and appears rational. This idea can be easily tested in the clinic.



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#### INITIAL REVIEW OF THE MANUSCRIPT

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**Manuscript NO:** 40147

**Title:** Exercise and glucagon-like peptide-1: Does exercise potentiate the effect of treatment?

**Reviewer’s code:** 01424366

**Reviewer’s country:** Canada

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-06-04

**Date reviewed:** 2018-06-05

**Review time:** 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This is a novel commentary on the possible ability of exercise to improve the ability of GLP-1 receptor agonists in T2D. This has not to my knowledge been addressed by other reviews. A strength of the paper is that it balances the data available concerning the



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possible effects of exercise on GLP-1 sensitivity vs. GLP-1 release. I think the review could be strengthened by more depth of speculation on possible contributing mechanisms of action of exercise. It is mentioned that microbiome changes result from exercise, and that this might alter GLP-1 release. Microbiome action on the digestion of dietary fibre results in the production of short-chain fatty acids (SCFA). SCFA interact with specific G-protein coupled receptors on the intestinal L-cells to modulate GLP-1 release. SCFAs also signal through the same receptors (GPR41 and GPR43) to increase glucose-stimulated insulin secretion from the beta cells. Hence, an effect of exercise on altering the microbiome could increase SCFA signaling to promote insulin release both through increased GLP-1 release and by a direct effect on the pancreas. On the other hand exercise can reduce adipokine release from adipose such as leptin, as well as reducing beta cell lipotoxicity, and improve both insulin sensitivity and beta cell function. The key pathway that needs examination is whether exercise improves GLP-1 sensitivity at a pancreatic or cardiovascular level to not only improve metabolic control, but also reduce diabetic complications. A fuller description of available knowledge on cellular pathways that might support this would enhance the review.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**Manuscript NO:** 40147

**Title:** Exercise and glucagon-like peptide-1: Does exercise potentiate the effect of treatment?

**Reviewer's code:** 00506294

**Reviewer's country:** Spain

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-06-04

**Date reviewed:** 2018-06-06

**Review time:** 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This editorial about an issue not well known as the efficacy of exercise on the GLP-1 secretion that is only partially investigated in patients with type 2 diabetes mellitus. The author considers that exercise appears to potentiate the effect of the GLP-1 receptor



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agonists treatment by ameliorating GLP-1 resistance and the gut microbiota in causing GLP-1 resistance. In addition, myokines are believed to play a vital role in mediating GLP-1 secretion/function during exercise. Although current evidence is limited, a human study demonstrated that a GLP-1 receptor agonist, exenatide, elevated irisin concentrations and enhanced the glycemic control in patients with type 2 diabetes mellitus. The editorial is well written and assess an item not well known with interest for the future treatment of type 2 diabetes mellitus.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**Manuscript NO:** 40147

**Title:** Exercise and glucagon-like peptide-1: Does exercise potentiate the effect of treatment?

**Reviewer’s code:** 03648962

**Reviewer’s country:** Pakistan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-06-04

**Date reviewed:** 2018-06-08

**Review time:** 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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**SPECIFIC COMMENTS TO AUTHORS**

This is an average manuscript, that can be published as is.

**INITIAL REVIEW OF THE MANUSCRIPT**



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**Manuscript NO:** 40147

**Title:** Exercise and glucagon-like peptide-1: Does exercise potentiate the effect of treatment?

**Reviewer’s code:** 02446617

**Reviewer’s country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-06-04

**Date reviewed:** 2018-06-09

**Review time:** 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This editorial addresses a very interesting and timely topic on how excersice may improve GLP1 signaling in patients with type 2 diabetes. I only have minor comments. The author should avoid the continous use conjunctive adverbs in the abstract and first



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paragraph. It is distracting. The abstract could benefit from addition of a summary sentence(s) that highlights the implications of the recommendations given in the editorial.

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