

Format for ANSWERING REVIEWERS



April 24, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8453-edited.doc).

Title: Targeting inflammation in diabetes: Newer therapeutic options

Author: NK Agrawal, Saket Kant

Name of Journal: *World Journal of Diabetes*

ESPS Manuscript NO: 8453

The manuscript has been improved according to the suggestions of reviewers:

Reviewer 1

| S.No | Comment | Correction |
|------|---|---|
| 1 | The English usage and grammar of the whole manuscript must be reviewed | Reviewed |
| 2 | Introduction: the aim of this review, and the methodology used to do it are lacking | The aim of this review is to elaborate on the drugs targeting inflammation in diabetes and its complications. Both previous studies and upcoming targets including their molecular mechanisms will be discussed in the review. |
| 3 | Inflammation and diabetes: this title suggests pathophysiology of inflammation in diabetes but in the last 3 paragraphs, you described drugs effects. Maybe you could add another item to describe the action on inflammation of drugs usually used in diabetic patients. | The mechanism of action of drugs on inflammatory pathways added at appropriate places (with each drug) |
| 4 | Newer therapeutic options: I missed a pattern of drugs descriptions, I mean class, mechanism of action, studies results, whether they're used or not and their indications. . And I suggest you to review the title because when you say | The title has been changed to newer therapeutic targets. These drugs are in trials for targeting inflammation and are not yet available as prescription drugs for diabetes-has been added. Class, mechanism of action, studies, results and the current status of the drugs also added. |

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| | “Newer therapeutic options”, it suggests that these are drugs that are already used to this proposal | |
| 5 | Other emerging therapies: It's not very clear how you selected the drugs to this group as you included glitazones | Glitazones have been removed from other emerging therapies and added alongside metformin as an anti-inflammatory drug. |
| 6 | Therapeutic treatments targeting inflammatory mediators in diabetic neuropathy/ nephropathy / retinopathy: I think it would be easier to the reader if you could begin briefly describing the mechanisms related to each complication and then results of studies using drugs directed to inflammation | The mechanism related to each complication along with their therapeutic implications added. |

Reviewer 2

| S.No | Comment | Correction |
|------|---|------------|
| 1 | Authors should comment and quote the fact that T2DM is part of the MS, of which NAFLD is the main factor | Added |
| 2 | What about non-alcoholic fatty liver disease as a new criterion to define metabolic syndrome? World J Gastroenterol. 2013 Jun 14;19(22):3375-84. doi: 10.3748/wjg.v19.i22.3375. PMID: 23801829 [PubMed - indexed for MEDLINE] | Added |
| 3 | The role of adiponectin in NAFLD. Should be evidenced and Authors | Added |

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| | <p>should quote : What is the role of adiponectin in obesity related non-alcoholic fatty liver disease?. World J Gastroenterol. 2013 Feb 14;19(6):802-12. doi: 10.3748/wjg.v19.i6.802. PMID: 23430039</p> | |
| 4 | <p>Authors should take into account that physical activity, linked to reduced expression of inflammatory cytokines is important in Diabetes-linked NAFLD.They should quote: Have guidelines addressing physical activity been established in nonalcoholic fatty liver disease?. World J Gastroenterol. 2012 Dec 14;18(46):6790-800. doi: 10.3748/wjg.v18.i46.6790.</p> | Added |
| 5 | <p>Authors should add the following approach, quoting: Omega-3 fatty acids for the treatment of non-alcoholic fatty liver disease. World J Gastroenterol. 2012 Nov 7;18(41):5839-47. doi: 10.3748/wjg.v18.i41.5839. PMID: 23139599.</p> | Added |
| 6 | <p>The umbalance between apoptosis and apoptosis in diabetes-linked NAFLD is important. authors shouls quote:Serum Bcl-2 concentrations in overweight-obese subjects with nonalcoholic fatty liver disease. World J Gastroenterol. 2011 Dec 28;17(48):5280-8. doi: 10.3748/wjg.v17.i48.5280.</p> | Added |

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| | PMID: 22219597 | |
| 7 | <p>The key link between IR and inflammation is expressed into the following papers that Authors should quote:</p> <p>JNKs, insulin resistance and inflammation: A possible link between NAFLD and coronary artery disease. World J Gastroenterol. 2011 Sep 7;17(33):3785-94. doi: 10.3748/wjg.v17.i33.3785. Review. PMID: 21987620</p> <p>[Spleen: A new role for an old player? World J Gastroenterol. 2011 Sep 7;17(33):3776-84. doi: 10.3748/wjg.v17.i33.3776. Review. PMID: 21987619</p> | Added |
| 8 | <p>Aurhors should not overlook the thromboembolism...and they should quote: High prevalence of nonalcoholic fatty liver in patients with idiopathic venous thromboembolism. Di Minno MN, Tufano A, Rusolillo A, Di Minno G, Tarantino G. World J Gastroenterol. 2010 Dec 28;16(48):6119-22. PMID: 21182227</p> | Added. |
| 9 | <p>Finally, the key links are the following that should be quoted. Hepatic steatosis, low-grade chronic inflammation and hormone/growth factor/adipokine imbalance. World J Gastroenterol. 2010 Oct</p> | Added |

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| | 14;16(38):4773-83. Hepatic steatosis in overweight/obese females: new screening method for those at risk. World J Gastroenterol. 2009 Dec 7;15(45):5693-9. PMID: 19960566 | |
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Thank you again for publishing our manuscript in the *World Journal of Diabetes*

Sincerely yours,

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