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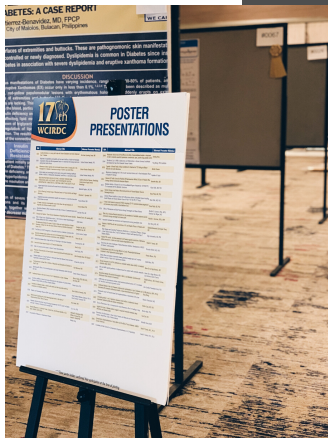


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- *Please, no more than 250 words!*
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- *Arial, 12 size font*

Title:

Example given: Adiponectin homolog novel osmotin protects obesity/diabetes-induced NAFLD by upregulating AdipoRs/PPAR α signaling in ob/ob and db/db transgenic mouse models

Author(s):

Example given: Ashfaq Ahmad, Tahir Ali, Min Woo Kim, Amjad Khan, Myeung Hoon Jo, Shafiq Ur Rehman, Muhammad Sohail Khan, Noman Bin Abid, Mehtab Khan, Rahat Ullah, Min Gi Jo, and Myeong Ok Kim, Ph.D.*

Affiliation:

Example given: Division of Applied Life Science (BK 21), College of Natural Sciences, Gyeongsang National University, Jinju, 660-701, Republic of Korea

Abstract:

Background: In metabolic disorders, adiponectin and adiponectin receptors (AdipoR1/R2) signaling has a key role in improving nonalcoholic fatty liver disease (NAFLD) in obesity-associated diabetes. **Objective:** To the best of our knowledge, here, we reported for the first time the underlying mechanistic therapeutic efficacy of the novel osmotin, a homolog of mammalian adiponectin, against NAFLD in leptin-deficient ob/ob and db/db mice. **Methods:** The ob/ob and db/db mice were treated with osmotin at a dose of 5 μ g/g three times a week for two weeks. To co-relate the in vivo results we used the human liver carcinoma HepG2 cells, subjected to knockdown with small siRNAs of AdipoR1/R2 and PPAR α genes and treated with osmotin and palmitic acid (P.A.). MTT assay, western blotting, immunohistofluorescence assays, and plasma biochemical analyses were applied. **Results:** Osmotin stimulated AdipoR1/R2 and its downstream APPL1/PPAR α /AMPK/SIRT1 pathways in ob/ob and db/db mice, and HepG2 cells exposed to P.A. Mechanistically, we confirmed that knockdown of AdipoR1/R2 and PPAR α by their respective siRNAs abolished the osmotin activity in HepG2 cells exposed to P.A. Overall, the in vivo and in vitro results suggested that osmotin protected against NAFLD through activation of AdipoR1/R2 and its downstream APPL1/PPAR- α /AMPK/SIRT1 pathways as shown by the reduced body weight, blood glucose level and glycated hemoglobin, improved glucose tolerance, attenuated insulin resistance and hepatic glucogenesis, regulated serum lipid parameters, and increased fatty acid oxidation and mitochondrial functions. **Conclusion:** Our findings strongly suggest that novel osmotin might be a potential novel therapeutic tool against obesity/diabetes-induced NAFLD and other metabolic disorders.

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Abbreviations (up to five):

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

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Funding:

This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

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Structured abstract:

A structured abstract, by means of appropriate headings, should provide the context or background for the research and should state its purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations.

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