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Corresponding author:

Itzen Aguniga Sanchez

liberitzen@yahoo.com.mx

Author Affiliation:

Universidad Nacional Autonoma de Mexico.

EFFICACY OF NARINGENIN IN THE REGULATION OF GLUCOSE AND LIPID PROFILE IN ANIMAL MODELS OF TYPE 2 DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Aguñiga-Sanchez, I¹; Ramos-Hernandez, Y²; Santiago-Osorio, E³; Rosado Perez, J⁴; Mendoza Nuñez, VM⁵; Alatraste-García, M⁶.

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2023 and was last updated on 26 October 2023.

INTRODUCTION

Review question / Objective What is the effect of naringenin administration on glucose regulation and lipid profile in animal models with type 2 Diabetes Mellitus?

P: Animal models of type 2 Diabetes Mellitus

I: Naringenin administration

C: Control (no treatment)

O: Glucose levels, insulin, Hb1Ac and lipid profile.

Rationale The World Health Organization (WHO) defines Diabetes Mellitus as a chronic disease that occurs when the pancreas does not produce enough insulin or when the body does not effectively use the insulin it produces, which leads to hyperglycemia and alterations in lipid metabolism. According to the International Diabetes Federation, Mexico ranks sixth in the world in people with diabetes. Medical treatment includes the indication of oral hypoglycemic agents or insulin. In this regard, it has been

reported that about 30% of diagnosed diabetics who are prescribed these drugs do not achieve or maintain glycemic and lipid control, as recommended by international standards, due to lack of therapeutic adherence and some side reactions. For this reason, alternative herbal and naturopathic treatments have been proposed. In this regard, medicinal plants and fruits are used worldwide for the treatment of diabetes and can provide a complementary or substitute alternative to allopathic drugs used, among which naringenin stands out; which is a flavonoid abundant in citrus plants, such as grapefruit and orange.

In some studies performed with diabetic rats, a hypoglycemic and hypolipidemic effect has been demonstrated after the administration of naringenin at different doses. Therefore, given the prevalence of diabetes, it is important to have a precise knowledge about the effect of naringenin on glucose and lipid metabolism from preclinical studies, which allows supporting the performance of clinical trials. In this sense, one of the best

methodological strategies is to carry out systematic reviews and meta-analyses, in accordance with the international PRISMA guidelines. It is worth mentioning as background, that in the literature there is a systematic review on the hypoglycemic effect of naringenin in animal models with diabetes mellitus in which only glucose is evaluated; there is also another systematic review where the cardioprotective effect of naringenin is evaluated, Therefore, the objective of this systematic review is to present a qualitative and quantitative analytical synthesis (meta-analysis) on the efficacy of naringenin in the regulation of glucose and lipid profile in animals with type 2 diabetes, according to PRISMA methodology.

Condition being studied Diabetes Mellitus type 2 (DM2) is a metabolic disease characterized by chronic hyperglycemia with alterations in carbohydrate, lipid and protein metabolism resulting from resistance to insulin actions in peripheral tissues, as well as inadequate insulin secretion and impaired suppression of glucagon secretion in response to ingested glucose. In 2019, it was estimated that 463 million adults aged 20-79 years worldwide (within this group, 9.3% of all adults) have Diabetes, 79.4% live in low- and middle-income countries. According to 2019 estimates, by 2030, 578.4 million adults aged 20-79 years are expected to have Diabetes; likewise, by 2045 the figure would increase to 700.2 million. The existence of an experimental animal model of a disease not only helps to understand its pathophysiology, but also the development of drugs for its treatment. Over the years, several animal models have been developed to study Diabetes Mellitus or test anti-diabetic agents.

METHODS

Search strategy A literature search was performed in the following scientific article platforms: PubMed; Scopus; Web of Science; ScienceDirect; LILACS; SciELO and as gray literature TESIUNAM. The following search strategy was used: (Naringenin) AND (Diabetes Mellitus type 2) AND (animal) NOT (human) NOT (review AND systematic review). A thesis search was also conducted to identify unpublished studies that could be included in the review. Once the titles and abstracts that met the selection criteria were selected, the full texts of articles potentially relevant to the review were retrieved and a comprehensive review was performed to.

Participant or population Animal models.

Intervention Oral administration of naringenin.

Comparator RATONES DIABETICOS.

Study designs to be included Tests in animal models.

Eligibility criteria - Trials conducted in animal models.- Oral administration of naringenin.- Comparison with a control group.- Evaluation of at least one of the following biochemical markers: serum levels of glucose, HbA1c, insulin, HDL, VLDL, LDL, cholesterol, triglycerides.

Information sources Database in the following scientific article platforms: PubMed; Scopus; Web of Science; ScienceDirect; LILACS; SciELO and as gray literature TESIUNAM.

Main outcome(s) We found 249 studies; 10 in PubMed; 74 in Scopus; 3 in Web of Science; 42 ScienceDirect; 41 in LILACS; 9 in SciELO and 4 in TESIUNAM, of which 17 met the criteria for quantitative analysis (systematic review) and 9 for quantitative analysis (meta-analysis).

Additional outcome(s) The results suggest that the administration of naringenin in rodents also has a hypolipidemic effect.

Data management EXCEL DATABASES WHERE THE SEARCHES OF THE CONSULTED DATABASES WERE REGISTERED, THE SELECTION WAS MADE BASED ON THE SELECTION CRITERIA. STUDIES THAT MET THE INCLUSION CRITERIA WERE SUBJECTED TO RISK OF BIAS ANALYSIS AND META-ANALYSIS.

Quality assessment / Risk of bias analysis Two reviewers assessed the risk of bias or methodological quality of each of the studies in animal models included in the review using Cochrane's SYRCLE scale, with which each study is judged on ten items, categorized into five groups: study selection, performance, attrition, reporting, and other bias.

Strategy of data synthesis IN THE QUALITATIVE ANALYSIS WE CONSIDERED THOSE STUDIES THAT MET THE INCLUSION CRITERIA AND FOR THE META-ANALYSIS WE SELECTED THOSE THAT COINCIDED IN DOSE, ROUTE OF ADMINISTRATION AND DURATION OF TREATMENT TO REDUCE THE PERCENTAGE OF HETEROGENEITY AND ANALYZED THEM IN THE REVIEW MANAGER 5.4.1 SOFTWARE.

Subgroup analysis SUBGROUPS WERE ANALYZED BY TIME OF TREATMENT AND DOSE.

Sensitivity analysis ALL THE DATA OBTAINED WERE USED.

Language restriction STUDIES IN ENGLISH, SPANISH AND PORTUGUESE WERE CONSIDERED.

Country(ies) involved MEXICO.

Keywords naringenin; animals; Diabetes Mellitus type 2.

Contributions of each author

Author 1 - ITZEN AGUÑIGA-SANCHEZ - Research, quantitative and qualitative analysis, writing of the article.

Email: liberitzen@yahoo.com.mx

Author 2 - Yolanda Ramos-Hernandez - Research , quantitative and qualitative analysis.

Email: ramosyh17@gmail.com

Author 3 - Edelmiro Santiago-Osorio - Article drafting and critical analysis.

Email: edelmiro@unam.com

Author 4 - Juana Rosado-Perez - Quantitative analysis, critical analysis and article drafting.

Email: juanarosadoperez@gmail.com

Author 5 - Victor Manuel Mendoza-Nuñez - I confirm findings of the search, analysis of results and discussion of the article.

Email: mendovic@unam.mx

Author 6 - Mariana Alatraste-García - Article writing and editing support.

Email: mariannalat18@gmail.com