



**UNIVERSIDAD NACIONAL DEL SUR**

**TESIS DE DOCTORA EN BIOLOGÍA**

**“Efectos de la administración oral de *Opuntia megapotamica*  
(Cactaceae) sobre la glucemia y los lípidos de ratas diabéticas”**

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## RESUMEN

Una de las patologías con mayor impacto en la sociedad mundial es la diabetes que está asociada a complicaciones a largo plazo que causan elevada morbi-mortalidad y su origen multifactorial incluye la desregulación del metabolismo de carbohidratos y de lípidos.

Se ha demostrado que numerosas hierbas y suplementos dietarios de origen vegetal poseen propiedades hipoglucemiantes e hipolipemiantes y mejoran el estado general del paciente diabético. Las plantas del género *Opuntia*, principalmente *Opuntia ficus-indica*, han sido y siguen siendo las más utilizadas, en particular en México. Con respecto a la especie nativa *Opuntia megapotamica*, hasta el presente no se ha evaluado su toxicidad ni se han llevado a cabo estudios que analicen sus potenciales propiedades medicinales.

El objetivo general de este trabajo de Tesis fue evaluar la toxicidad y los efectos de las harinas de cladodios, de pulpa de frutos y de semillas de *Opuntia megapotamica* sobre la glucemia y los lípidos de ratas normales y diabéticas a través de la realización de estudios *in vivo* en los cuales se administró, por vía oral, diferentes dosis de las harinas de la planta. Además, se analizó el contenido y la composición de los lípidos de las harinas de cladodios y de semillas.

De los ensayos de toxicidad aguda y sub-aguda se determinó que la harina de pulpa no posee efectos tóxicos mientras que las harinas de cladodios

y de semillas generan algunas alteraciones histológicas en el hígado y en el riñón que no se traducen en modificaciones en los parámetros bioquímicos ni en cambios en el comportamiento y en el estado general de los animales.

La caracterización lipídica de las harinas de cladodios y de semillas, realizada por primera vez en esta especie de *Opuntia*, indica que la primera por su elevado contenido en ácidos grasos poliinsaturados podría tener un potencial valor nutracéutico.

Con respecto a los efectos sobre la glucemia, se estableció que las tres harinas tienen una marcada acción anti-hiperglucemiante en ratas normales con hiperglucemia transitoria mientras que el suministro de las harinas de cladodios y de semillas, durante 30 días, no modifica la glucemia basal en ratas diabéticas. Sin embargo, en estas últimas se observó un leve aumento en los niveles plasmáticos de insulina que podría indicar un incipiente efecto benéfico de la planta sobre el páncreas.

En cuanto a los lípidos, se registró un importante efecto hipolipemiante a nivel plasmático, hepático y renal. Solo la harina de cladodios modifica la actividad de las enzimas hepáticas HMG-CoA reductasa y ácido graso sintasa, claves en la biosíntesis de colesterol y de ácidos grasos, respectivamente.

La administración de las harinas de cladodios y de semillas produce marcados efectos positivos sobre el funcionamiento del hígado y una leve tendencia al mejoramiento de la función renal.

En conjunto, los resultados obtenidos de estos estudios pre-clínicos aportan una información original y muy útil que puede servir como base para futuros estudios clínicos que permitan sustentar el empleo de *Opuntia megapotamica* como recurso terapéutico.

## ABSTRACT

Diabetes, one of the pathologies with greatest impact on society worldwide, is associated with long-term complications ending in high morbidity and mortality. Its multifactorial origin includes carbohydrate and lipid metabolism deregulation.

It has been demonstrated that several herbs and dietary vegetal supplements which have hypoglycemic and hypolipidemic properties improve the general conditions of diabetic patients. Plants from *Opuntia* genus, mainly *Opuntia ficus-indica*, have been and still are the most used, specially in México. As to the native species *Opuntia megapotamica*, no studies have been conducted to date to evaluate its toxicity and its potential medicinal properties.

The general objective of this Thesis work was to evaluate *Opuntia megapotamica* toxicity and the effects that cladode, fruit pulp and seed flours exert on glycemia and lipids in normal and diabetic rats. To this end, *in vivo* studies were carried out in which different doses of cladodes, fruits pulp and seeds were orally administered. The content and composition of lipids from cladode and seed flours were also analyzed.

Results from the analyses focused on acute and sub-acute toxicity reveal that whereas fruit pulp flour has no toxic effects, flours from cladodes and seeds produce some histological alterations in liver and kidney which have no correlations with changes in biochemical parameters or in the behavior and general condition of the animals studied.

The lipid characterization of cladode and seed flours, carried out for the first time in this *Opuntia* species, suggests that because of the high polyunsaturated fatty acid content cladode flour could have a potential nutraceutical value.

As to *Opuntia megapotamica* glycemic effects, it was determined that whereas its three flour types have an important anti-hyperglycemic action in normal rats with transient hyperglycemia, cladode and seed flours administration, during 30 days, does not modify basal glycemia in diabetic rats. In the latter, a slight increase in insulin plasmatic levels was registered and it could indicate an incipient plant beneficial effect on the pancreas.

Very important hypolipemiant effects in plasma, liver and kidney lipids were also determined. Only cladode flour was observed to modify the activity of the hepatic enzymes HMG-CoA reductase and fatty acid synthase, both of which have key roles in cholesterol and fatty acid synthesis, respectively.

The administration of cladode and seed flours produces not only significant positive effects on liver functioning but also a slight tendency to improve renal function.

Taken together, the results collected from these pre-clinical studies provide original and useful data that can serve as basis for future clinical research that will enable sustain the use of *Opuntia megapotamica* as a therapeutic tool.

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