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**UNIVERSIDADE ESTADUAL PAULISTA
“JÚLIO DE MESQUITA FILHO”
FACULDADE DE MEDICINA**

Rafaianne Queiroz de Moraes Souza

**Repercussões bioquímicas e reprodutivas de
mães e descendentes após o consumo materno
de dieta hiperlipídica em roedores: Revisão
Sistemática**

Tese apresentada à Faculdade de Medicina, Universidade Estadual Paulista “Júlio de Mesquita Filho”, Campus de Botucatu, para obtenção do título de Doutora em Ginecologia, Obstetrícia e Mastologia.

Orientadora: Profa. Dra. Débora Cristina Damasceno
Coorientador: Prof. Dr. Gustavo Tadeu Volpato

Botucatu
2019

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Botucatu
2019

FICHA CATALOGRÁFICA ELABORADA PELA SEÇÃO TÉC. AQUIS. TRATAMENTO DA INFORM.
DIVISÃO TÉCNICA DE BIBLIOTECA E DOCUMENTAÇÃO - CÂMPUS DE BOTUCATU - UNESP
BIBLIOTECÁRIA RESPONSÁVEL: ROSANGELA APARECIDA LOBO-CRB 8/7500

Souza, Rafaienne Queiroz de Moraes.

Repercussões bioquímicas e reprodutivas de mães e descendentes após o consumo materno de dieta hiperlipídica em roedores : revisão sistemática / Rafaienne Queiroz de Moraes Souza. - Botucatu, 2019

Tese (doutorado) - Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Medicina de Botucatu

Orientador: Débora Cristina Damasceno

Coorientador: Gustavo Tadeu Volpato

Capes: 40101150

1. Dieta hiperlipídica. 2. Animais. 3. Prenhez. 4. Estresse oxidativo. 5. Revisão.

Palavras-chave: Dieta hiperlipídica; animais; perfil bioquímico; prenhez.

*“Sou feita de retalhos.
Pedacinhos coloridos de cada vida que passa pela minha e que
vou costurando na alma.
Nem sempre bonitos, nem sempre felizes, mas me acrescentam
e me fazem ser quem eu sou.
Em cada encontro, em cada contato, vou ficando maior...
Em cada retalho, uma vida, uma lição, um carinho, uma
saúde...
Que me tornam mais pessoa, mais humana, mais completa.*

*E penso que é assim mesmo que a vida se faz: de pedaços de
outras gentes que vão se tornando parte da gente também.
E a melhor parte é que nunca estaremos prontos, finalizados...
Haverá sempre um retalho novo para adicionar à alma.*

*Portanto, obrigada a cada um de vocês, que fazem parte da
minha vida e que me permitem engrandecer minha história
com os retalhos deixados em mim. Que eu também possa deixar
pedacinhos de mim pelos caminhos e que eles possam ser parte
das suas histórias.*

*E que assim, de retalho em retalho, possamos nos tornar, um
dia, um imenso bordado de nós”.*

Cris Pizzimenti

Dedicatórias

A Deus por toda graça e misericórdia infinita, pelo amor e cuidado de cada segundo.

“Porque dEle e por Ele, e para Ele, são todas as coisas; glória, pois, a Ele eternamente” (Romanos 11:36)

À minha família, por todo apoio, carinho e ensinamentos, tudo que sou devo a vocês. Especialmente ao meu filho, Miguel Queiroz M. Souza, que chegou a este mundo me ensinando que sempre é preciso lutar!

“A família é o amor de Deus nos oferecendo um pouquinho do céu aqui na Terra.” (Autor desconhecido)

Agradecimentos

Ao meu esposo, **Bruno Andrade de Souza**, que escolheu sonhar este sonho comigo, sempre esteve ao meu lado. Por todo incentivo, amparo e carinho, muito obrigada!

Ao meu filho amado, **Miguel Q. M Souza**, pelo amor, carinho e hoje ser a maior alegria da minha vida.

À minha mãe, **Maria Joana Queiroz**, por ser meu maior exemplo e me ensinar que devemos lutar por nossos sonhos.

À minha sogra, **Maria das Graças Andrade de Souza**, por ser solícita e viajar 800 Km para cuidar do meu filho sempre que necessário, permitindo que eu pudesse estudar tranquilamente, nunca poderei retribuir tudo o que a senhora fez por nós!

Ao meu Coorientador, **Prof. Dr. Gustavo Tadeu Volpato**, por ser mais que um professor em minha vida, um “pai científico”, um amigo querido. Sempre serei grata pelos anos de convivência e me lembrarei que só cheguei até aqui pela primeira oportunidade que recebi.

À minha orientadora, **Profa. Dra. Débora C. Damasceno**, obrigada por se preocupar não só pelo meu aprendizado, mas também por questões pessoais. Nunca esquecerei das perguntas: Vocês estão com frio? Fome? Onde irão dormir? Serei eternamente grata, por ter este sentimento maternal e por sempre desejar o melhor para nós. Todos os ensinamentos me tornaram uma profissional e ser humano melhor.

À minha amiga e parceira de longa data, **Thaigra de Sousa Soares**, por estar ao meu lado nesta jornada, obrigada por tudo.

À **Vêronyca de Paula Gonçalves**, por ter mudado seus planos e decido a nos ajudar, não encontro palavras suficientes para expressar minha gratidão.

À **Giovana Vesentini**, por todo tempo, ensinamento e paciência. Este trabalho se tornou possível por meio das suas contribuições.

À profa. Dra. **Yuri Karen Sinzato**, por compartilhar conhecimentos, pela amizade e por ser um exemplo para mim.

À minha família **FISIOTOX** (professores **Gustavo Tadeu Volpato**,

Kleber Eduardo de Campos e Madileine F. Américo e todos os alunos), não poderei citar todos os nomes, porque durante quase 10 anos muitos passaram por lá e marcaram a minha vida, obrigada não só pelas discussões e reuniões científicas, mas pelos cafés e conversas do dia-a-dia.

Aos meus **colegas e amigos do LAPGO**, aos que já saíram e os que ainda permanecem, obrigada por me acolherem e permitir que eu fizesse parte também desta família.

Aos meus amigos **Eduardo Kloppel, Carolina A. Miranda, Verônyca P. Gonçalves, Rosa Jacinto Volpato, Nágilla Orleane**, por me abrigar, pela amizade e carinho para comigo.

À **Mariana Pirani e Larissa Lopes**, por compartilhar conhecimentos, pela amizade e cada palavra de incentivo.

Aos animais **Pizza, Dristy, Lex, Madona e Brotinho**, que me acolheram em seus lares e sempre me receberam com carinho.

À **Carolina Saullo**, por compartilhar conhecimento sobre constituição dietética.

Aos assistentes de suporte acadêmico (ASA) da Unidade de Pesquisa Experimental (UNIPLEX) da Faculdade de Medicina de Botucatu, especialmente aos Srs. **Danilo Chaguri, Carlos Roberto Gonçalves de Lima, José Márcio Cândido e Jurandir Antônio**, pela manutenção dos biotérios, limpeza e cuidados com os animais. Apesar deste trabalho não ser uma pesquisa original, participo de outros projetos. Então, agradeço por todo auxílio. Muito obrigada!

À Faculdade de Medicina de Botucatu – Unesp, em especial ao **Laboratório de Pesquisa Experimental de Ginecologia e Obstetrícia (LAPGO)**, por todos os recursos dispensados a mim.

Aos funcionários da Seção de **Pós-graduação da Faculdade de Medicina de Botucatu**, em particular à secretária do Programa de Pós-graduação em Ginecologia, Obstetrícia e Mastologia, **Sra. Solange Sako Cagliari**, obrigada por ser sempre solícita e pelos auxílios prestados.

Ao **Escritório de Apoio à Pesquisa (EAP)** da Faculdade de Medicina de

Botucatu, Unesp, pelo serviço prestado. Em especial ao **Prof. Dr. José Eduardo Corrente**, pelos cálculos e análises estatísticas para os projetos que correram em paralelo a esta revisão sistemática.

À **equipe da biblioteca da Unesp de Botucatu** pela confecção da ficha catalográfica e outros auxílios realizados.

À **Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)**, pela concessão da bolsa, permitindo total dedicação a execução desse estudo.

A todos aqueles que contribuíram direta ou indiretamente para a realização deste trabalho. Obrigada por todos os gestos singelos ou grandiosos. É necessário ser grato, porque ninguém caminha sozinho!

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Capítulo 1

1. CONSIDERAÇÕES INICIAIS

Este estudo faz parte de um projeto mais amplo intitulado “Avaliação de descendentes expostas ao diabetes moderado intrauterino, submetidas à dieta hiperlipídica no período pós-natal e tratadas com mistura de cálcio e vitamina D durante a prenhez” (Protocolo CEUA 1218/2017). Obteve financiamento da FAPESP (Processo número 2016/25207-5, vigência de 01/07/2018 a 30/06/2020).

No primeiro projeto elaborado como sendo o doutorado de Rafaianne Queiroz Moares Souza, a metodologia contemplava os estudos sobre o útero materno e parâmetros fetais referente os animais do projeto completo descrito acima. Para obtenção de filhas de diabéticas (FDmod) com idade adulta, são necessários pelo menos 180 dias (meio ano). Ao longo deste experimento, foi observado que as ratas FDmod apresentaram dificuldades para acasalamento, o que retardou o tratamento desses animais, bem como o experimento como um todo. Após o segundo ano de tentativas frustradas para obtenção de ratas prenhes, advindas de ambiente intrauterina hiperglicêmico e alimentadas com dieta hiperlipídica, a aluna obteve uma pequena amostragem de animais prenhes. Estes animais foram tratados, mas durante o experimento, todos os animais prenhes e não-prenhes foram a óbito em virtude de uma contaminação bacteriana, confirmada por exames específicos realizados no Laboratório Clínico do Hospital Veterinário da FMVZ – Unesp. Desta forma, a aluna precisou reiniciar todo o experimento para obtenção de todos os grupos experimentais. No entanto, como a aluna ainda está coletando os dados novamente

para apresentação desta tese foi realizada uma revisão sistemática a respeito deste assunto. Os resultados sobre prenhez e tratamento com vitamina D e/ou cálcio continuam em andamento e estarão sob a responsabilidade desta aluna e de outras estudantes envolvidas no projeto completo para que sejam tabulados, analisados, discutidos e, posteriormente, publicados em revista de âmbito internacional.

2. ATIVIDADES EXECUTADAS DURANTE O DOUTORADO

A aluna iniciou o Doutorado em março de 2015, durante todo esse período participou das atividades desenvolvidas no Laboratório de Fisiologia de Sistemas e Toxicologia Reprodutiva (FISIOTOX) da Universidade Federal do Mato Grosso (UFMT) e no Laboratório de Pesquisa Experimental em Ginecologia e Obstetrícia (LAPGO), pertencente ao Programa de Pós-graduação em Ginecologia, Obstetrícia e Mastologia da Faculdade de Medicina de Botucatu, Universidade Estadual Paulista (UNESP).

2.1 Artigos Publicados

2.1.1. Soares TS, Andreolla AP, Miranda CA, Klöppel E, Rodrigues LS, **Moraes-Souza RQ**, Damasceno DC, Volpato GT, Campos KE. Effect of the induction of transgenerational obesity on maternal-fetal parameters. *Syst Biol Reprod Med.* 2018; 64(1):51-59.

Effect of the induction of transgenerational obesity on maternal-fetal parameters

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ABSTRACT

Maternal obesity can cause complications for both women and their offspring for generations. Therefore, we intended to verify the repercussions of induction of transgenerational obesity on biochemical parameters, reproductive performance, and congenital anomaly frequency in Wistar rats. Female rats were used from successive generations. The female rats of parental generation (F₀, n=10) were mated to obtain their offspring (F₁ generation). F₁ female rats received a monosodium glutamate (MSG) solution to induce obesity (n=07) or vehicle (control, n=06) during the neonatal period. These adult female rats were classified as normal or obese using the Lee Index, mated, and delivered offspring (F₂ generation), which were also evaluated for obesity using the Lee Index in adult life (F₂MSG, n=13, born from obese dams) or non-obesity status (F₂Control, n=12, born from control dams), and were mated in adulthood. During pregnancy, glycemia and an oral glucose tolerance test (OGTT) were analyzed. At term pregnancy, the females were sacrificed for serum biochemical profile, maternal reproductive outcomes, and fetal development. In F₂MSG rats, body weight gain at early pregnancy, glycemia by OGTT, total cholesterol, high-density-lipoprotein, and alanine transaminase activity were higher compared with those of F₂Control rats. F₂MSG rats also presented a lower implantation number and gravid uterus weight, increased pre-implantation loss and anomaly frequency in their fetuses (F₃ generation) compared with those of F₂Control rats. Therefore, even without significant changes in body weight gain, obesity was established at the end of pregnancy of Wistar rats using other biomarkers. Additionally, these rats showed multiple adverse reproductive outcomes, confirming the deleterious effects that lead to obesity.

ARTICLE HISTORY

Received 4 July 2017
Revised 12 November 2017
Accepted 13 November 2017

KEYWORDS

Fetus; obesity; rat;
transgenerational

Introduction

Obesity and its related comorbidities have become one of the main conditions negatively impacting public health, representing an alarming global problem. The epidemic proportions of obesity are mainly resulting from lifestyle changes, including increased high calorie intake and decreased physical activities [Flegal et al. 2015]. Obesity and being overweight have also increased in women of reproductive age [McDonald et al. 2010], and have increased strongly in populations with low and average incomes, especially in urban areas of developed countries [Nelson et al. 2010]. During pregnancy, obesity can cause complications for both women and their offspring, which may result in still-birth and congenital anomalies [Begum et al. 2011]. The impaired maternal intrauterine environment may

induce critical changes in fetal growth and development, contributing to the risk of developing disease in later life [Barker 2007; Gluckman et al. 2008].

Clinical and experimental studies show that maternal obesity induced intrauterine changes may influence the fetal organism leading to metabolic adaptations and/or complications [Gluckman et al. 2008], such as glucose intolerance, obesity, and metabolic syndrome in adult life [Barker 2007; Campos et al. 2007; Desai et al. 2013]. Obese women present an increased risk of birth defects in their offspring [Stothard et al. 2009]. In experimental models, obesity is related to an abnormal biochemical profile, with obese rats presenting with increased serum triglyceride levels and glucose intolerance in their offspring [Chen et al. 2014].

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2.1.2. Afiune LAF, Leal-Silva T, Sinzato YK, **Moraes-Souza RQ**, Soares TS, Campos KE, Fujiwara RT, Herrera E, Damasceno DC, Volpato GT. Beneficial effects of *Hibiscus rosa-sinensis* L. flower aqueous extract in pregnant rats with diabetes. PLoS One. 2017; 12(6):e0179785.

RESEARCH ARTICLE

Beneficial effects of *Hibiscus rosa-sinensis* L. flower aqueous extract in pregnant rats with diabetes

Luana Alves Freitas Afiune¹, Thais Leal-Silva¹, Yuri Karen Sinzato², Rafaienne Queiroz Moraes-Souza^{1,2}, Thaigra Sousa Soares^{1,2}, Kleber Eduardo Campos¹, Ricardo Toshio Fujiwara³, Emilio Herrera⁴, Débora Cristina Damasceno², Gustavo Tadeu Volpato^{1,2*}

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 OPEN ACCESS

Citation: Afiune LAF, Leal-Silva T, Sinzato YK, Moraes-Souza RQ, Soares TS, Campos KE, et al. (2017) Beneficial effects of *Hibiscus rosa-sinensis* L. flower aqueous extract in pregnant rats with diabetes. PLoS ONE 12(6): e0179785. <https://doi.org/10.1371/journal.pone.0179785>

Editor: Ying-Ju Lin, China Medical University, TAIWAN

Received: February 24, 2017

Accepted: June 4, 2017

Published: June 23, 2017

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Data Availability Statement: All relevant data are within the paper.

Funding: Ricardo T. Fujiwara and Débora C. Damasceno received support from Conselho Nacional de Desenvolvimento Científico e Tecnológico.

Competing interests: The authors have declared that no competing interests exist.

Abstract

Purpose

The *Hibiscus rosa-sinensis* flower is widely used in Brazilian traditional medicine for the treatment of diabetes and has shown antifertility activity in female Wistar rats. However, there is no scientific confirmation of its effect on diabetes and pregnancy. The aim of this study was evaluate the effect of aqueous extract of *H. rosa-sinensis* flowers on maternal-fetal outcome in pregnant rats with diabetes.

Methods

Diabetes was induced by streptozotocin (STZ, 40 mg/kg) in virgin, adult, female Wistar rats. After diabetes induction, the rats were mated. The pregnant rats were distributed into four groups (n minimum = 11 animals/group): non-diabetic, non-diabetic treated, diabetic, and diabetic treated. Oral aqueous extract of *Hibiscus rosa-sinensis* was administered to rats in the treatment groups during pregnancy. At term pregnancy, maternal reproductive outcomes, fetal parameters, and biochemical parameters were analyzed.

Results

The non-diabetic treated group showed decreased high density lipoprotein cholesterol, increased atherogenic index (AI) and coronary artery risk index (CRI), and increased preimplantation loss rate compared to the non-diabetic group. Although treatment with *H. rosa-sinensis* led to no toxicity, it showed deleterious effects on cardiac and reproductive functions. However, the diabetic treated group showed increased maternal and fetal weights,

2.1.3. **Moraes-Souza RQ**, Reinaque AP, Soares TS, Silva AL, Giunchetti RC, Takano MA, Akamatsu MA, Kubrusly FS, Lúcio-Macarini F, Raw I, Iourtov D, Ho PL, Bueno LL, Fujiwara RT, Volpato GT. Safety evaluation of a vaccine: Effect in maternal reproductive outcome and fetal anomaly frequency in rats using a leishmanial vaccine as a model. PLoS One. 2017; 12(3):e0172525 (**Publicação referente à Dissertação de Mestrado**).



RESEARCH ARTICLE

Safety evaluation of a vaccine: Effect in maternal reproductive outcome and fetal anomaly frequency in rats using a leishmanial vaccine as a model

Rafaelle Q. Moraes-Souza^{1*}, Ana Paula Reinaque^{2*}, Thaígra S. Soares¹, Ana Luiza T. Silva², Rodolfo C. Giunchetti³, Maria A. S. Takano⁴, Milena A. Akamatsu⁴, Flávia S. Kubrusly⁴, Fernanda Lúcio-Macarini⁴, Isaias Raw⁴, Dmitri Iourtov⁴, Paulo Lee Ho⁴, Lilian L. Bueno², Ricardo T. Fujiwara², Gustavo T. Volpato^{1*}

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OPEN ACCESS

Citation: Moraes-Souza RQ, Reinaque AP, Soares TS, Silva AL, Giunchetti RC, Takano MAS, et al. (2017) Safety evaluation of a vaccine: Effect in maternal reproductive outcome and fetal anomaly frequency in rats using a leishmanial vaccine as a model. PLoS ONE 12(3): e0172525. doi:10.1371/journal.pone.0172525

Editor: Henk D. F. H. Schallig, Academic Medical Centre, NETHERLANDS

Received: August 26, 2016

Accepted: February 6, 2017

Published: March 1, 2017

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This work was supported by: Rafaelle Q. Moraes-Souza received CAPES (Coordenação de Aperfeiçoamento Pessoal de Nível Superior) scholarship; Ana Paula Reinaque received CAPES (Coordenação de Aperfeiçoamento Pessoal de Nível Superior) - DINTER allowance; part of this study was supported by grants from FAPEMIG

Abstract

While the immunogenic potential of the vaccination against infectious diseases was extensively shown, data on the safety assessment of recombinant proteins in vaccine formulations administered during pregnancy are still scarce. In the current study, the antigenicity of a vaccine against leishmaniasis (based on *Leishmania braziliensis* recombinant protein peroxidoxin) during pregnancy and possible maternal reproductive outcomes and fetal anomalies after immunization with a leishmanial vaccine or adjuvant alone (*Bordetella pertussis* derived MPLA adjuvant) were assessed. Rats were mated and allocated in three groups: **Control**—rats received saline; **Adjuvant**—rats received the adjuvant MPLA, and **Vaccine**—rats received the combination of MPLA and peroxidoxin. The administration was subcutaneously at the dorsal region, three times (days 0, 7, 14 of pregnancy). On day 21 of pregnancy, all rats were bled for biochemical and immunological measurements. The gravid uterus was weighed with its contents, and the fetuses were analyzed. The immunization with peroxidoxin induced a significant production of circulating IgG levels compared to other groups but caused a significant in post-implantation loss (14.7%) when compared to Control (5.0%) and Adjuvant (4.4%) groups. Furthermore, a significantly high rate of fetal visceral anomalies, such as hydronephrosis and convoluted ureter, was also observed in animals that received vaccine when compared to Control or Adjuvant groups. These data indicate the importance of safety evaluation of vaccines during pregnancy and the limited use of peroxidoxin administration during pregnancy. More importantly, the safety monitoring of immunization with MPLA derived from *Bordetella*

2.1.4. Pinheiro MS, Rodrigues LS, S L Neto, **Moraes-Souza RQ**, Soares TS, Américo MF, Campos KE, Damasceno DC, Volpato GT. Effect of *Bauhinia holophylla* treatment in streptozotocin-induced diabetic rats. An Acad Bras Cienc. 2017; 89(1):263-272.



Anais da Academia Brasileira de Ciências (2017) 89(1): 263-272
(Annals of the Brazilian Academy of Sciences)
Printed version ISSN 0001-3765 / Online version ISSN 1678-2690
<http://dx.doi.org/10.1590/0001-3765201720160050>
www.scielo.br/aabc

Effect of *Bauhinia holophylla* treatment in Streptozotocin-induced diabetic rats

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Manuscript received on January 27, 2016; accepted for publication on November 28, 2016

ABSTRACT

Bauhinia holophylla, commonly known as “cow’s hoof”, is widely used in Brazilian folk medicine for the diabetes treatment. Therefore, the aim of this study was at evaluating the aqueous extract effect of *Bauhinia holophylla* leaves treatment on the streptozotocin-induced diabetic rats. Diabetes was induced by Streptozotocin (40 mg/Kg) in female Wistar rats. Oral administration of aqueous extract of *Bauhinia holophylla* leaves was given to non-diabetic and diabetic rats at a dose of 400 mg/kg during 21 days. On day 17 of treatment, the Oral Glucose Tolerance Test was performed to determine the area under the curve. At the end of the treatment, the animals were anesthetized and blood was collected for serum biochemical parameters analysis. After treatment with *Bauhinia holophylla* extract, non-diabetic and diabetic rats presented no glycemic changes. On the other hand, the plant treatment decreased body weight and increased ALT and AST activities. In conclusion, the treatment with aqueous extract of *B. holophylla* leaves given to diabetic rats presented no hypoglycemic effect in nondiabetic animals and no antidiabetic effect in diabetic animals with the doses studied. In addition, the diabetic animals treated with the *B. holophylla* extract showed inconvenient effects and its indiscriminate consumption requires particular carefulness.

Key words: *Bauhinia holophylla*, diabetes, lipid profile, medicinal plants, rats.

INTRODUCTION

Diabetes mellitus is the name given to a group of disorders with different etiologies. It is characterized by disarrangements in carbohydrates, proteins and fat metabolism caused by complete or partial insufficiency of insulin secretion and/or insulin action (ADA 2016, Reece et al. 2004).

Several drugs are used to control diabetes, however, perfect glucose control is rarely achieved

(Cooppan 2005). Moreover, plants have been used as an alternative therapy for the diabetes treatment. Many plants present hypoglycemic activity, which were demonstrated experimentally in animals and humans, but some still require further investigation (Volpato et al. 2002, Damasceno and Volpato 2008). Although several plants were tested for diabetes treatment, many of them were not evaluated, including species of the genus *Bauhinia*, popularly known as “cow’s hoof” (Lorenzi and Matos 2002). These species typically present a wide distribution

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2.1.5. **Moraes-Souza RQ, Soares TS, Carmo NO, Damasceno DC, Campos KE, Volpato GT. Adverse effects of *Croton urucurana* B. exposure during rat pregnancy. J Ethnopharmacol. 2017;199:328-333 (Publicação referente à Monografia).**

Journal of Ethnopharmacology 199 (2017) 328–333



Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep



Adverse effects of *Croton urucurana* B. exposure during rat pregnancy



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ARTICLE INFO

Keywords:
Croton urucurana
Plant
Toxicity
Malformation
Pregnancy

ABSTRACT

Ethnopharmacological relevance: Several women often use plant extracts during pregnancy without any concern about its possible toxic effects. The plant effects have been experimentally confirmed in animals and humans, while others require additional investigations.

Aim of study: To evaluate the effect of aqueous extract of *Croton urucurana* latex on the maternal-fetal repercussions in rats.

Methods: Pregnant rats were randomly distributed into four experimental groups: Control=treated with water (vehicle); Treated 200=treated with a dose 200 mg/kg; Treated 400= dose 400 mg/kg and; and Treated 800= dose 800 mg/kg. The rats were orally treated by gavage with *Croton urucurana* or vehicle (water) during whole pregnancy. At term of pregnancy, all rats were killed to obtain maternal blood and tissues samples and fetal weight and anomaly analyses.

Results: *C. urucurana* treatment (Treated 400 and Treated 800) showed elevated liver enzymatic activities, reduced fetal body weight and placental efficiency. The Treated 800 group presented increased maternal total protein and cholesterol levels, and heart relative weight. All treated groups presented reduced maternal body weight and food intake, and increased pre-implantation loss rate compared to those of Control group. In addition, the treatment contributed to increased skeletal and visceral anomalies with higher doses.

Conclusion: *Croton urucurana* treatment caused maternal toxicity, which contributed for impairment embryo fetal development. These results showed that the indiscriminate use of plants during pregnancy should be avoided to prevent potential risk on maternal health as well as their offspring.

1. Introduction

Medicinal plants have been widely used to treat a variety of diseases. However, the use of these plants during pregnancy may present health risks to the woman and also to her fetus (Moreira et al., 2014). Certain herbs, used as abortifacients can induce embryotoxicity, fetotoxicity and/or teratogenicity when embryonic death does not occur. *Croton urucurana* Bailon, popularly known as dragon blood, blood water, capixingui, urucuana, lucurana, tapexingui and tapixingui, is considered an abortive plant (Gurgel et al., 2002). *Croton* is a large and diverse genus of Euphorbiaceae that comprises at least 800 species of the tropics and subtropics (Webster, 1993). *C. urucurana* is widespread in wetlands and riparian areas and is commonly found in southern Brazil, northern Argentina, Paraguay and Uruguay. The *C. urucurana* tree has an open canopy and bright stem, and reaches up to 15 m (Babieri et al., 2014).

The indigenous culture believe that *C. urucurana* shows remarkable healing properties. This plant has been extensively used in folk medicine for treatment of cancer, rheumatism, lesions, ulcers, diarrhea infections (Rao et al., 2007). Three different products from *C. urucurana* species are primarily used - the red sap or latex, stem bark and the gum exudate (Simionatto et al., 2007). In male rats, Esmeraldino et al. (2005) found that the stem bark of *C. urucurana* aqueous extract showed anti hemorrhagic activity. Also in male rats, was observed an anti-diarrheal response after treatment with 600 mg/kg of *C. urucurana* latex (Gurgel et al., 2001), and antifungal activity against five different dermatophytes when using *C. urucurana* sap in an in vitro study (Gurgel et al., 2005). Cordeiro et al. (2012), testing the acute toxicity of this plant, demonstrated that a single dose of 2000 mg/kg of *C. urucurana* bark methanol extract produced no toxicity signs in female rats, whereas doses at 50, 100 and 250 mg/kg caused reduced gastric lesions in male rats. In 2016, these same

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<http://dx.doi.org/10.1016/j.jep.2016.10.061>

Received 6 July 2016; Received in revised form 17 October 2016; Accepted 19 October 2016

Available online 20 October 2016

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2.1.6. Damasceno DC, Leal-Silva T, Soares TS, **Moraes-Souza RQ**, Volpato GT. Medicinal plants for diabetes treatment during pregnancy. *Curr Med Chem*. 2017; 24(4):404-410.

Current Medicinal Chemistry, 2017, 24, 404-410

REVIEW ARTICLE



Medicinal Plants for Diabetes Treatment During Pregnancy



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Abstract: *Diabetes mellitus* is a syndrome of great importance that affects an increasing number of people every day. In particular, diabetes is a common and important disease during pregnancy and is marked by complications, both fetal and maternal, that increase the risks of morbidity and mortality for diabetic pregnant women and their offspring. Drugs such as insulin and hypoglycemic drugs are given to treat diabetes, but regular exercise and adequate diet have also been indicated. Furthermore, coadjuvant therapies such as medicinal plants are popularly used to reduce diabetes-induced hyperglycemia, either within or outside the context of pregnancy. However, studies examining plant use for diabetes treatment are necessary to confirm its possible effects and its safety for the mother and fetus. The objective of this literature review was to conduct a survey of plant species that are utilized worldwide and their stated therapeutic uses. A literature search was performed using the terms “diabetes and pregnancy”, which resulted in the identification of 31,272 articles. Of these studies, only 12 (0.0038%) were related to medicinal plants, demonstrating that there has been little investigation into this issue. Of the papers analyzed in this review, half evaluated plant leaves, indicating that these scientific studies attempted to reproduce the preparations commonly used by various populations, i.e., in the form of tea. Additionally, more than 90% of studies utilized experimental animals to evaluate the maternal-fetal safety of medicinal plant substances that may potentially be dangerous for humans. Thus, once confidence levels for plant-derived substances are established based on toxicological analyses and safety is confirmed, it is possible that plants will be used to complement conventional diabetes therapies.

ARTICLE HISTORY

Received: March 24, 2016
Revised: July 12, 2016
Accepted: July 22, 2016

DOI: 10.2174/092986732366161003122914

Keywords: *Diabetes mellitus*, pregnancy, medicinal plants, herbs, treatment, review.

1. DIABETES BY THE NUMBERS

Diabetes mellitus is a complex and chronic disease that requires continuous medical care to reduce blood glucose and multifactorial risks. It presents multiple etiologies characterized by the chronic elevation of fasting and/or post-prandial glucose due to absolute or relative defects in insulin synthesis or decreased effects of insulin [1, 2].

Diabetes is a crucially important syndrome that is becoming the epidemic of the century. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population [3]. In the Americas, the number of individuals with diabetes was estimated at 35 million in 2000 and projected to be 64 million in 2025 [4]. However, as of 2011, that number reached 62.8 million and is expected to reach 91.1 million in 2030 [5]. Diabetes is among the ten major causes of death in Western countries, and despite progress in clinical management, its lethal consequences still cannot be prevented. In

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2.2 Apresentação de pôsteres em congressos nacionais e internacionais

- 2.2.1. MORAES-SOUZA, R. Q.; CRUZ, L. L.; SOARES, T.S.; PAULA, V. G.; SINZATO, Y. K.; DAMASCENO, D. C.; VOLPATO, G. T. “Effects of *Curatella americana* treatment on complications of diabetic pregnancy”. In: 6th International Symposium on Metabolic Programming and Microbiome and 3rd Meeting of Ibero-American DOHaD chapter, 2018, Cancun. Book of abstracts, 2018. v. 1. p. B60008.
- 2.2.2. MORAES-SOUZA, R.Q.; REINAQUE, A. P. B.; SOARES, T.S.; BUENO, L. L.; FUJIWARA, R. T.; VOLPATO, G. T. “Repercussões maternas de ratas vacinadas com proteína peroxidoxina recombinante de *Leishmania braziliensis* durante a prenhez”. In: I Workshop do Programa de Imunologia e Parasitologia Básicas e Aplicadas, 2015, Barra do Garças. Livro de Resumos, 2015. v. 1. p. 11-11.
- 2.2.3. MORAES-SOUZA, R.Q.; NETO, L.S.; ALVES, D. G.; SOARES, T.S.; CAMPOS, K. E.; AMERICO, M.F.; DAMASCENO, D. C.; VOLPATO, G. T. “Effect of *Hancornia speciosa* aqueous extract treatment on biochemical parameters in diabetic pregnant rats”. In: XX Congresso da Sociedade Brasileira de Diabetes, 2015, Porto Alegre. Diabetology & Metabolic Syndrome, 2015. v. 7. p. A76.

Além das apresentações e participações em congresso, a aluna foi coautora de outros 36 resumos publicados em anais.

2.3 Participações em bancas de trabalhos de conclusão de curso

- 2.3.1. Participação em banca de Thalita Bohnen Carneiro. Efeitos materno-placentário-fetais em diferentes intensidades glicêmicas no início da prenhez dentro do modelo experimental

de diabetes moderado, 2016 (Enfermagem) Universidade Federal de Mato Grosso.

2.3.2. Participação em banca de Bruno Stephano Ferreira da Silva. Repercussões fetais do tratamento com *Curatella americana* em ratas prenhes com diabetes de intensidade moderada, 2018 (Enfermagem) Universidade Federal de Mato Grosso.

2.4 Coorientações concluídas de alunos

2.4.1. Vanessa Caruline Araujo da Silva. Repercussões maternas e fetais de ratas tratadas com Micofenolato de Sódio antes da prenhez. 2016. Orientador: prof. Dr. Gustavo Tadeu Volapto. Nível: iniciação científica.

2.4.2. Cristielly Maria Barros Barbosa. Efeitos adversos do tratamento com Ciclosporina antes e durante a prenhez. 2016. Orientador: prof. Dr. Gustavo Tadeu Volapto. Nível: Iniciação Científica.

2.4.3. Mário Cezar Fiuza Carlos. Repercussões maternas e fetais de ratas tratadas com Tacrolimo antes da prenhez. 2015. Orientador: prof. Dr. Gustavo Tadeu Volapto. Nível: Iniciação Científica.

2.5 Atividades de ensino

Atuação como professora convidada para ministrar o tema "Placentação e Anexos embrionários". Disciplina de Histologia e Embriologia, cursos de Graduação Enfermagem e Biomedicina. Carga horária: 4 horas. Período: 2016, 2018 e 2019.