“PHARMACOLOGICAL EFFECTS AND SAFETY PROFILE FOLLOWING ADMINISTRATION OF OPUNTIA ELATIOR FRUIT JUICE AND QUERCETIN IN DIABETIC RATS”

By

KOTADIYA CHINTU RAMESHBHAI

(Registration No: J4-01496-2014)  
B.V.Sc. & A.H.

DEPARTMENT OF VETERINARY PHARMACOLOGY AND TOXICOLOGY
COLLEGE OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY
JUNAGADH AGRICULTURAL UNIVERSITY
JUNAGADH - 362 001

JULY- 2016
"PHARMACOLOGICAL EFFECTS AND SAFETY PROFILE FOLLOWING ADMINISTRATION OF OPUNTIA ELATOR FRUIT JUICE AND QUERCETIN IN DIABETIC RATS"

A

THESIS SUBMITTED TO THE JUNAGADH AGRICULTURAL UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF

MASTER OF VETERINARY SCIENCE

IN VETERINARY PHARMACOLOGY AND TOXICOLOGY

KOTADIYA CHINTU RAMESHBHAII

(Registration No: J4-01496-2014)

B.V.Sc. & A.H.

DEPARTMENT OF VETERINARY PHARMACOLOGY AND TOXICOLOGY COLLEGE OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY JUNAGADH AGRICULTURAL UNIVERSITY JUNAGADH - 362 001

JULY - 2016
"PHARMACOLOGICAL EFFECTS AND SAFETY PROFILE FOLLOWING ADMINISTRATION OF OPUNTIA ELATIOR FRUIT JUICE AND QUERCETIN IN DIABETIC RATS"

A THESIS SUBMITTED TO THE JUNAGADH AGRICULTURAL UNIVERSITY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF VETERINARY SCIENCE IN VETERINARY PHARMACOLOGY AND TOXICOLOGY BY KOTADIYA CHINTU RAMESHBHAI (Registration No: J4-01496-2014) B.V.Sc & A.H.

DEPARTMENT OF VETERINARY PHARMACOLOGY AND TOXICOLOGY COLLEGE OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY JUNAGADH AGRICULTURAL UNIVERSITY JUNAGADH - 362 001 JULY - 2016
DEDICATED TO ANIMALS, MY GUIDE & MY ALL FAMILY MEMBERS
ABSTRACT

Diabetes mellitus describes a metabolic disorder of carbohydrate metabolism characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is one of the slowly progressive disorders identified by Indian Council of Medical Research which as alternative medicine is a need for the present. Literature on the pharmacological properties of different varieties of Opuntia species presented the present study was carried out to evaluate the pharmacological safety profile following administration of Opuntia elatior fruit juice to diabetic rats. Fortytwo Albino rats were randomly divided into seven groups (C1, C2, C3, C4, T1, T2 and T3). C1 and C2 were kept as normal, vehicle and distance control groups respectively. Group C3 were injected phloroisoflavone to induce diabetes, and C3 were kept as control, vehicle and distance control groups respectively. Group C3 were administrated with glibizide 15 mg/kg, P.O. for 16 days. Rats of group T1 and T2 were injected with Opuntia elatior fruit juice (4 ml/kg, P.O.) and aqueous (20 mg/kg, P.O.) respectively for 25 days. Rats of group T3 were administrated with Opuntia elatior fruit juice along with quercetin for 25 days. The changes in blood sugar, clinical symptoms of diabetes were observed in these groups. These symptoms were mild in comparison to those observed in group C3.

In lipid profile, levels of total cholesterol and triglyceride were significantly increased while levels of HDL cholesterol and LDL cholesterol were non-
ABSTRACT

Keywords: Albino rat, Opuntia elatior fruit juice, Quercetin, Antidiabetic effect, Safety profile, Hyperalgesic activity, Spontaneous motor activity

Diabetes mellitus describes a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. It is one of refractory diseases identified by Indian Council of Medical Research for which an alternative medicine is a need for the treatment. Looking to the pharmacological properties of different varieties of Opuntia spp. and quercetin, the present study was carried out to evaluate the pharmacological effects and safety profile following administration of Opuntia elatior fruit juice and quercetin in diabetic rats. Forty two albino rat were randomly divided based on blood glucose level in seven groups (C1, C2, C3, C4, T1, T2 and T3). Rats of five groups (C3, C4, T1, T2 and T3) were injected streptozotocin to induce diabetes. Rats of group C1, C2, and C3 were kept as normal, vehicle and diabetic control, respectively. Rats of group C4 were administrated with glibenclamide (5 mg/kg, P.O. for 28 days). Rats of group T1 and T2 were treated with Opuntia elatior fruit juice (4 mL/kg, P.O.) and quercetin (50 mg/kg, P.O.) respectively for 28 days. Rats of group T3 were administrated with Opuntia elatior fruit juice along with quercetin for 28 days. After induction of diabetes, clinical symptoms of diabetes were observed in rats of diabetic control group. These symptoms were mild to moderate in all other treatment group compare to diabetic control group.

In lipid profile, levels of total cholesterol and triglyceride were significantly increased while levels of HDL-cholesterol and LDL-cholesterol were non-
significantly higher in diabetic control group compared to other groups. The mean levels of total cholesterol, HDL-cholesterol and LDL-cholesterol in rats treated with quercetin along with Opuntia elatior were found comparable to normal control rats. In hematological parameters, mean values of Hb (g/dL), packed cell volume (%) and total erythrocyte count (10⁶/μl) in rats of diabetic control were significantly (P<0.05) lower compared to other groups. Mean values of MCHC (%), and MCH (pg) in rats of diabetic control were significantly (P<0.05) higher compared to other groups. Whereas, the mean value of above parameters in rats treated with Opuntia elatior fruit juice alone (T1) was significantly (P<0.05) higher than those of the other treatment groups. Rats treated with quercetin alone and in combination with Opuntia elatior fruit juice were similar to or higher than mean values of same parameters in rats of control groups. In biochemical parameters, mean values of ALT, AST and creatinine non-significantly increased while, the mean values LDH was significantly higher in rats of diabetic control group compare to normal control groups. The mean values of total protein, albumin, globulin, total bilirubin, BUN and ALP were found non-significant in all groups compared to control rats.

Upon gross examination of pancreas, no appreciable gross lesions in all treatment groups have been observed. Macroscopic examination of liver and kidneys of experimental rats of diabetic control group shown congestion, paleness and mild to moderate enlargement. No remarkable changes have been observed in other group. The histopathological changes of pancreas of rats of diabetic control group (C3) revealed varying degree of structural changes as well as degenerative changes. Liver of rats of diabetic control group (C3) revealed varying degree of degenerative changes, vascular changes and infiltration of inflammatory cells with loss of normal architecture of parenchyma and changes in kidney were also observed in rats of diabetic control group. No appreciable histopathological lesions have been observed in the spleen, intestine, heart and lung of rats in all treatment groups.

In conclusion, routine administration of Opuntia elatior and quercetin can improve glucose and lipid profile level in diabetic rats. Though the findings of this short term study are encouraging further detailed investigation is required to determine the effect of long term administration of Opuntia elatior and quercetin in diabetic rats.
COLLEGE OF VETERINARY SCIENCE & A. H. 
JUNAGADH AGRICULTURAL UNIVERSITY
JUNAGADH

CERTIFICATE-I

This is to certify that the thesis entitled “PHARMACOLOGICAL EFFECTS AND SAFETY PROFILE FOLLOWING ADMINISTRATION OF OPUNTIA ELATIOR FRUIT JUICE AND QUERCETIN IN DIABETIC RATS” submitted by KOTADIYA CHINTU RAMESHBHAI in partial fulfillment of the requirements for the award of the degree of MASTER OF VETERINARY SCIENCE, in the subject of VETERINARY PHARMACOLOGY AND TOXICOLOGY to Junagadh Agricultural University is a record of bonafied research work carried out by her under my guidance and supervision and the thesis has not previously formed the basis for the award of any degree, diploma or other similar title. The candidate had fulfilled all prescribe requirements. The assistance and help received during the course of investigation have been fully acknowledged. She has successfully completed the comprehensive/preliminary examination held on November 2, 2015 as required under the regulation for post-graduate studies. She has submitted kachchha bound thesis on 27/05/2016.

Place: Junagadh
Date: 27/05/2016

(U.D. Patel)
Major Guide
Associate Professor & Head
Department of Veterinary Pharmacology & Toxicology
College of Veterinary Science & A.H.
Junagadh Agricultural University
Junagadh
COLLEGE OF VETERINARY SCIENCE & A. H.
JUNAGADH AGRICULTURAL UNIVERSITY
JUNAGADH

CERTIFICATE-II

Date: 08/07/2016

This is to certify that the thesis entitled “PHARMACOLOGICAL EFFECTS AND SAFETY PROFILE FOLLOWING ADMINISTRATION OF OPUNTIA ELATION FRUIT JUICE AND QUERCETIN IN DIABETIC RATS” submitted by Miss. CHINTU R. KOTADIYA to Junagadh Agricultural University, Junagadh in partial fulfillment of the requirements for the degree of MASTER OF VETERINARY SCIENCE in the subject of VETERINARY PHARMACOLOGY AND TOXICOLOGY after recommendation by the external examiner were defended by the candidate before the following members of the examination committee. The performance of the candidate in the oral examination was satisfactory. We therefore recommend that the thesis be approved.

(U. D. Patel)  
Major Guide  
Associate Professor & Head  
Dept. of Vet. Pharmacology & Toxicology  
College of Veterinary Science & A.H.  
J. A. U., Junagadh

(V. A. Kalaria)  
Minor Guide  
Assistant Professor  
Dept. of Veterinary Pathology  
College of Veterinary Science & A.H.  
J. A. U., Junagadh

(K. A. Sadariya)  
External examiner  
Assistant Professor  
Dept. of Vet. Pharmacology & Toxicology  
College of Veterinary Science & A.H.,  
A. A.U., Anand

(U. D. Patel)  
Associate Professor & Head  
Dept. of Vet. Pharmacology & Toxicology  
College of Veterinary Science & A.H.  
J. A. U., Junagadh

(J. S. Patel)  
I/C Principal & Dean  
College of Veterinary Sci. & A.H.  
J. A. U., Junagadh

Approved by

(V. P. Chovatia)  
Director of Research & Dean P.G. Studies  
Junagadh Agricultural University, Junagadh
ACKNOWLEDGEMENT

I shall ever remain thankfully indebted to all those learned souls, my present and former teachers, whose untiring hands taught me directly or indirectly to achieve my goal and enlightened me with the touch of their knowledge and constant encouragement. I feel this is an extremely significant and precious opportunity bestowed upon me by the goddess of learning, to thank about and thank all these persons.

I express deepest gratitude and appreciation to my Major Guide, Dr. V. B. Patel, Associate Professor and Head, Department of Pharmacology and Toxicology, College of Veterinary Science & Animal Husbandry, Junagadh Agricultural University, Junagadh, for his scholastic guidance, patient planning, keen interest, constant critical supervision, excellent cooperation, and invaluable control throughout the pursuit of this study. His very cordial behavior would always remain a beacon light for me in future also.

I take this opportunity to express my heartfelt thanks to my Minor Guide, Dr. V. A. Kalatra, Assistant Professor, Department of Veterinary Pathology, College of Veterinary Science & Animal Husbandry, Junagadh, for continuous encouragement and indispensable suggestions and interest during the study and research period.

I wish to express my deepest thanks and appreciation to Dr. D. B. Tantri, Principal and Dean, College of Veterinary Science and Animal Husbandry, Junagadh, for providing research facilities and an opportunity to pursue my higher studies in such an enviable institute of Gujarat state.

I am also thankful to Dr. A. V. Desai, Director of Animal and Plant Health Studies, IAUS, Junagadh, and Dr. N. K. Bhoombhetkar, Head of the Department of Pharmacognosy, for allowing me to stay in their laboratory.

I owe equally gratitude to the members of advisory committee, Dr. R. S. Patel, Associate Professor, Department of Pharmacology and Toxicology, College of Veterinary Science & Animal Husbandry, Junagadh, for their able guidance and encouragement.

ACKNOWLEDGEMENT
ACKNOWLEDGEMENT

I shall ever, remain thankfully indebted to all those learned souls, my present and former teachers, known and unknown hands who directly or indirectly motivated me to achieve my goal and enlightened me with the touch of their knowledge and constant encouragement. I feel this is an extremely significant and joyous opportunity bestowed upon me by the goddess of learning, to think about and thank all those persons.

I express deepest gratitude and appreciation to my Major Guide, Dr. U. D. Patel, Associate Professor and Head, Department of Pharmacology and Toxicology, College of Veterinary Science & Animal Husbandry, Junagadh Agricultural University, Junagadh for his scholastic guidance, prudent planning, keen interest, constant critical supervision, excellent cooperation and invaluable counsel throughout the pursuit of this study. His very cordial behavior would always remain beacon light for me in future also.

I take this opportunity in expressing my heartfelt thanks to my Minor Guide Dr. V. A. Kalaria, Assistant Professor, Department of Veterinary Pathology, College of Veterinary Science & Animal Husbandry, JAU, Junagadh for continuous motivation and indispensable suggestions and counsel during the study and research period.

I wish to express my deepest thanks and appreciation to Dr. P. H. Tank, Principal and Dean, College of Veterinary Science and Animal Husbandry, Junagadh for providing Research facilities and an opportunity to pursue my higher studies from such an esteemed institute of Gujarat state.

I am also thankful to Dr. A. Y. Desai, Director of Research and Dean, PG studies, JAU, Junagadh and Dr. N. K. Dhamsaniya, Registrar, JAU, Junagadh for allowing M. V. Sc. study and providing me all facility for research work.

I am equally grateful to the members of advisory committee Dr. H. B. Patel, Assistant Professor, Department of Pharmacology and Toxicology, College of Veterinary Science & Animal Husbandry, Junagadh Agricultural University,
Junagadh and Dr. B. B. Javia, Assistant Professor and Head, Department of Veterinary Microbiology, College of Veterinary Science & Animal Husbandry, JAU, Junagadh for their invaluable and critical suggestions, which served as a constant source of inspiration throughout the course of my study and research work.

I also express my deep gratitude to Dr. C. M. Modi, Assistant Professor, Department of Pharmacology and Toxicology, College of Veterinary Science & Animal Husbandry, Junagadh Agricultural University, Junagadh for his continuous support and motivation during this work.

I fail in words to express my earnest thanks to Dr. V. G. Bhalani, who always kept me under shade of their affection and given me inspiration throughout my college life.

I am very much thankful to Dr. D. T. Fefar, Assistant Professor, Department of Veterinary Pathology, College of Veterinary Science & Animal Husbandry, JAU, Junagadh and Dr. A. R. Bhadania, Assistant Professor and Head, Department of Veterinary Pathology, College of Veterinary Science & Animal Husbandry, JAU, Junagadh for their support during the pathological evaluation of samples and indispensable suggestions and counsel during the study and research period.

I am thankful to Dr. Satish Patel, Group leader, Zydus Research Centre, Cadila Healthcare Ltd., Ahmedabad, Gujarat, for providing albino rats and guiding to develop diabetic animal model used in the study.

I am highly thankful to Dr. R. J. Padodara, Assistant Professor and Head, Dept. of Veterinary Physiology and Biochemistry and Dr. H. H. Savasani Associate Professor and Head, Department of Animal Nutrition, College of Veterinary Science & Animal Husbandry, JAU, Junagadh for providing the laboratory facilities to undertake the research and there needful help during my study period.

I am highly obliged and grateful to Shri Punit Bhatt, Research Associate, Kajal Pandya, Senior Research Fellow, Shri Vadarbhai, Lab. Tech, Department of Veterinary Pharmacology and Toxicology, and Ankita Jani, Lab. Tech, Department of Veterinary Pathology, College of Veterinary Science & Animal Husbandry, JAU, Junagadh for necessary help whenever needed during the entire study period.

I am immensely thankful to my colleagues Dr. Vipul Chauhan, Dr. Shradhha Vekariya, Dr. Hetal Jivani, Dr. Chandani Pandavadara, Dr. Dhaval Vaghela, and...
Dr. Trushen Shah, for their kind co-operation and unreserved help during the course of study.

I feel pleasure to express my thanks to Jayantibhai for their help during my research work.

It is like a drop in the ocean of words that can never reach its mark to acknowledge infinite love, blessings, sacrifices and constant encouragement of my beloved parents Shri Rameshbhai P. Kotadiya and Smt. Bhavnaben R. Kotadiya, my brother Sandip and my sisters Dr. Bhumi & Ruchika who have been the sole source of inspiration for me to proceed ahead in my life.

Above all, I thank Almighty God for his blessings.

Finally, I am deeply indebted to all animals whose precious lives were sacrificed during this research work.

Last but not least, I owe gratitude and thankfulness to all who were involved directly or indirectly, knowingly or unknowingly to reach in the venture of mine.

Place: JUNAGADH
Date: 24/05/2016

(Kotadiya Chintu R.)