ملخص مشروع رسالة ماجستير-٣

عنوان المشروع باللغة العربية	تأثير الفلافونويد الغذائي، نارينجنين، على الإجهاد التأكسدي في شبكية العين السكري في الجرذان
English /عنوان المشروع باللغة الإنجليزية	Effect of dietary flavonoid, naringenin, on the oxidative stress status and inflammation in diabetic rat retina
Advisor /المشرف الرئيس	Professor Abdullah S. Alhomida
Minor Specification /التخصص الدقيق للمشرف الرئيس	Enzymes and Medical Biochemistry
Co-Advisor /المشرف المساعد	Dr Shams Ulola
المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا	10-12 months
Abstract or synopsis of the proposal (200 words or less):	Diabetic retinopathy (DR) is a severe complication of diabetes and is the leading cause of blindness among working adults worldwide. DR is being widely recognized as a neurodegenerative disease of the retina, since, retinal neurons are vulnerable to be damaged early in the disease progression. Diabetic induced oxidative stress is widely considered as the major cause of oxidative damage in diabetic retina. Oxidative damage may cause neurodegeneration early in diabetic retina which may lead to diabetic retinopathy. In this study, we will employ polyphenolic compound, naringenin to treat streptozotocin-induced diabetic rats and analyzed the inhibitory factors of oxidative stress and inflammation in the retina. We will measure the level of free radicals, level of glutathione as antioxidant in the diabetic and non-diabetic retina with and without naringenin treatments. We utilize ELISA and immunoblotting experiments to determine the level of ICAM1, MCP1, TNFa and IL1b in those retinal samples. Our analyses would indicate the beneficial effect of naringenin treatment in amelioration of oxidative stress and inflammation in the retina of diabetic rats.
Hypothesis or scientific justification of the proposal	Diabetic retinopathy is a severe complication of diabetes that develops slowly and is common in patient with diabetes. Diabetic induced oxidative stress is widely considered as the major cause of oxidative damage in

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	diabetic retina. Oxidative damage may cause neurodegeneration early in diabetic retina which may lead to diabetic retinopathy. Free radicals produced in excess culminate in neurodegeneration. Therapeutic approaches have shown that supplementation with antioxidants that reduce oxidative stress may play an important role in the treatment of diabetic neurological complications. Polyphenolic compounds are known for their strong antioxidant activities. Naringenin is a flavanone, a type of flavonoid, which is considered to have a bioactive effect on human health as antioxidant, free radical scavenger. Thus, the purpose of this study was to utilize naringenin as a therapeutic drug which may be effective against diabetes induced oxidative stress, inflammation and dysregulated neurotrophic factors responsible for damaging retinal neurons in diabetes.
Specific objectives	To Analyze of the effect of naringenin on the oxidative stress and inflammation in diabetic rat retina.
Methodology and Major Techniques to be used	Three months aged male Wistar albino rats, weighing 250–270 g will be injected single dose of streptozotocin (65 mg/kg body weight) made in citrate buffer intraperitoneally to make rats diabetic. Diabetes will be confirmed after 3 days by measuring fasting blood glucose level more than 300 mg/dl For drug treatments, animals will be divided into four groups (n = 6) as follows; (1) control (C), (2) control treated with naringenin (C+N) (2) diabetic (D), (3) diabetic treated naringenin at a dose 100 mg/kg/day (D+N), administered orally by gavage to those rats. Vehicle and naringenin treatments will be started once a day, after 1 week of diabetes induction and continued for five consecutive weeks. All procedures including euthanasia were conducted in accordance with the institutional guidelines of of the Experimental Animal Care Center, King Saud University and approval

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	from ethical committee. At the end of the treatments, animals will be fasted overnight and blood samples will be collected though cardiac puncture under deep anesthesia, retinas will be quickly removed, rinsed in ice-cold saline and homogenized in a cold 50 mM phosphate-buffered saline (pH 7.4) containing 1 % triton X-100, 0.2 % SDS, and a protease inhibitor cocktail by short burst of sonication. The homogenates will be then centrifuged at 10,000 rpm for 15 min at 4^{o}C. We will measurements of reactive oxygen species (ROS) using a derivative of reduced fluorescein (from Molecular Probes) carboxy-H_2DCFDA. We will also measure the level of oxidative stress by measuring the level of glutathione with or without naringenin treatments in the retina of those diabetic and nondiabetic rats. Glutathione will be measured by Ellman's method. We will measure the effect of naringenin on inflammatory markers in the retina of those treated and untreated diabetic and control rats. We will use ELISA and immunoblotting techniques to measure ICAM1, MCP1, TNFa and IL1b in those retinal samples.
Availability of Samples	Samples would be available from animals, after approval from ethical committee of the use animal in this proposal.
Availability of Chemicals	YES ◉ NO ○
Availability of Instruments	YES ◉ NO ○
Availability of Ethical Approval (if needed)	YES ○ NO ◉ Required, Yes, after Bioethical Committee approval of the use of animal, we will make rats diabetic and then will obtain retinal samples
Project Funded	YES ◉ NO ○
Recent References	1. M. Shamsul Ola, Nawaz M, Ahsan H (2011) Role of Bcl-2 family proteins and caspases in the regulation of apoptosis. Mol Cell Biochem. 351(1-2):41-58. 2. M. Shamsul Ola, Nawaz MI, Siddiquei

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