2)

عنوان المشروع باللغة العربية - Title of the proposed project in Arabic	التأثير الوقائي للكيوريسيتين على التسمم الكلوي الناتج عن بروميت البوتاسيم في الفئران
Title of the proposed project in English	Protective effect of quercetin on potassium bromate induced nephrotoxicity in rats
المشرف الرئيس - PI	Dr Nikhat J Siddiqi
التخصص الدقيق للمشرف الرئيس - Specialty of PI	Collagen biochemistry and oxidative stress /antioxidants
المشرف المساعد - Co-PI	Dr Nouf O Alafaleq
المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected time in month to finish	12
Abstract of the proposal (No more than 200 words)	Potassium bromate (KBrO3) is a food additive that is used as a maturing agent for flour and as a dough conditioner. It is also used in cosmetics and in the disinfection of drinking water. Exposure to KBrO3 results in multiple organ toxicity with kidney being the primary target organ of this compound. KBrO3 alters gene expression in renal tissues and chronic administration of KBrO3

	induces carcinomas in rats, hamsters and mice (Ahmad et al., 2015). Quercetin, is a flavonoid naturally occurring in plant extracts and phytochemicals. It also exhibits a wide range of biological functions including anti-carcinogenic, anti-inflammatory, antiviral, and psychostimulant activities, in addition to the ability to inhibit lipid peroxidation, platelet aggregation and capillary permeability, and to stimulate mitochondrial biogenesis (Aguirre, et al , 2011). In the proposed study the protective effect of quercetin on KBrO3 induced oxidative stress in rat kidneys will be studied.
Hypothesis of the proposal	Potassium bromate (KBrO3) is known to exert its toxic effect through the generation of oxidative stress. Quercetin being an antioxidant plant flavanoid would afford protection against KBrO3 induced nephrotoxicity. So the proposed study is expected to answer this hypothesis.
Specific objectives	1. Investigate the mechanism of KBrO3 induced toxicity. 2. To see the protective effect of quercetin on KBrO3 induced toxicity.
Methodology & Major Techniques to be used	Part I: This will consist of four groups of rats. Each group will consist of ten rats. Group 1- will consist of ten rats which will serve as control. Group 2- rats given a single dose of KBrO3 at 100 mg/kg body weight sacrificed 12 hours after the injection. Group 3- rats given a single dose of KBrO3 at 100 mg/kg body weight sacrificed 24 hours after the injection. Group 4- rats given a single dose of KBrO3 at 100 mg/kg body weight sacrificed 48 hours after the injection. Part II: This will consist of following groups of rats each consisting of ten rats. Group 1- rats receiving quercetin 20 mg/kg body weight. Group 2- rats receiving quercetin 50 mg/kg body weight for five days. Group 3- rats receiving quercetin 20 mg/kg body weight for five days followed by a single dose of KBrO3(100 mg/kg body) after six hours. Group 4- rats receiving quercetin 50 mg/kg body weight (depending upon the survival) for five days followed by a single dose of KBrO3(100 mg/kg body) after six hours. The animals will be sacrificed after 48 hours of last treatment. The serum from the animals will be used to determine blood urea nitrogen (BUN) and creatinine. The kidneys will be dissected out and used for biochemical analysis.

	1. Lipid peroxidation will be Lipid peroxidation was determined by the method of Utley, Berheim et al. (1967). 2. Reduced glutathione will be estimated by the method of Beutler, Duron et al. (1963). 3. Protein carbonyl levels in the samples was quantified as per the l method Levine, Garland et al. (1990). 4. Glutathione reductase activity will be assayed by the method developed by Goldberg and Spooner (1987). 5. Superoxide dismutase will be estimated by the method of Kakkar, Das et al. (1984). 6. Catalase was assayed by the method Aebi (1984). 7. The protein content in the sample was measured by the modified method of Lowry Markwell, Haas et al. (1978) 8. Advanced oxidation protein products will be measured by the method of Witko et al., 1992. 9. Quantitation of DNA fragmentation will be done by the colorimetric diphenylamine assay.
Availability of Samples	No
Kindly justify	The animals will be dosed after the approval of the project and ethical approval.
Availability of Chemicals	No
Kindly justify	They will be purchased upon approval of the project and fund sanction.
Availability of Instruments	Yes

Ethical Approval	In the process
Recent References	Ahmad MK, Khan AA, Ali SN, Mahmood R. Chemoprotective effect of taurine on potassium bromate-induced DNA damage, DNA-protein cross-linking and oxidative stress in rat intestine. PLoS One. 2015 Mar 6;10(3):e0119137. doi: 10.1371/journal.pone.0119137. eCollection 2015. Aguirre, L., Arias, N., Macarulla, M. T., Gracia, A., & Portillo, M. P. (2011). Beneficial effects of quercetin on obesity and diabetes. Open Nutraceuticals J, 4, 189-198. Beutler E, Duron O, Kelly BM (1963). Improved method for the determination of blood glutathione. J Lab Cli. Med ; 61: 882-888. Burton K. A study of the conditions and mechanism of the diphenylamine reaction for the colorimetric estimation of deoxyribonucleic acid. Biochem J. 1956; 62: 315–322. PMID: 13293190 Burton K. A study of the conditions and mechanism of the diphenylamine reaction for the colorimetric estimation of deoxyribonucleic acid. Biochem J. 1956; 62: 315–322. Goldberg, D.M., Spooner, R.J (1987). Glutathione reductase. NAD(P)H: oxidized Glutathione oxidoreductase (EC 1.6.4.2), third ed. In: Bergmeyer, H.U.,Bergmeyer, J., Graßi, M. (Eds.), Methods of Enzymatic Analysis, vol. III Verlag Chemie, Weinheim. 258–265. Kakkar P, Das B, Viswanathan PN. A modified spectrophotometric assay of superoxide dismutase. Indian J Biochem Biophys. 1984 Apr;21(2):130-2. Levine RL, Garland D, Oliver C, Amici A, Climent I, Lenz A (1990) . Determination of carbonyl content in oxidatively modified proteins. Methods Enzymol. 186:464–478. Markwell MAK, Haas SM, Bieber LL, Tolbert NE (1978) . A modification of the Lowry procedure to simplify protein determination im membrane and lipoprotein samples. Anal Biochem . 87: 206-210. Quantitation of DNA fragmentation will be done by the colorimetric diphenylamine assay by the method of Burton K, 1956. Utley HG, Berheim F, Hochstein P (1967). Effect of sulfhydryl reagent on peroxiation in microsomes. Arch Biochem Biophys. 118: 29-32. V. Witko, A.T. Ngugen, L.A. Descampus, Microtiter plate assay for phagocytic derived chloramines, Journal of Clinical and Laboratory Analysis 61 (1992), 46–53.