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ANTI-INFLAMMATORY AND ANTI-OXIDANT EFFECT OF RUTIN ON 2, 4, 6-TRINITROBENZENE SULFONIC ACID INDUCED ULCERATIVE COLITIS IN RATS.

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ABSTRACT

In the present study, the potential protective and therapeutic effect of rutin (RUT) administration on serum nitric oxide (NO), tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), colon tissue lipid peroxidation, antioxidant enzymes, reduced glutathione (GSH), and myeloperoxidase (MPO) in trinitrobenzene sulfonic acid (TNBS)-induced ulcerative colitis in rats have been evaluated. Fourty male albino rats were divided into four equal groups of 10 rats each. Group I :(Control group): received no drugs. Group II :(ulcerative colitis -induced group): Administered single intra-colonially dose of 150 mg/kg of TNBS for ulcerative colitis induction. Group III :(ulcerative colitis + RUT protected group): received RUT (200 mg/kg body weight/day) orally for 21 days prior TNBS administration for ulcerative colitis induction. Group IV :(ulcerative colitis + RUT treated group): treated with RUT as in group III for 21 days after ulcerative colitis induction. Blood samples and colon tissue were collected at the 22th day from the onset of RUT administration. The obtained results showed that, TNBS-induced ulcerative colitis caused significant decreased in serum NO level and Glutathione peroxidase (GPx), Superoxide dismutase (SOD), Glutathione –S- transferase (GST) and catalase (CAT) activities in colon tissue. On the other hand, a marked increase in colon tissue Glutathione reductase (GR) and MPO activities and GSH and L-Malondialdehyde (L-MAD) concentrations and in serum TNF-α and IL-1β levels were observed in TNBS induced colitis in rats. Rutin was able to mitigate colon mucosa damage induced by TNBS through increasing of NO, GPX, SOD, CAT, and GST in addition to decreasing L-MDA, TNF-α, IL-1β and MPO activity in colon tissue. These results suggest that, rutin may be effective in enhances the healing of ulcerative colitis by its radical scavenging and anti-inflammatory effect, inhibited neutrophil accumulation, and regenerating endogenous antioxidant mechanisms.

Keywords: Rutin; TNBS; Colitis; Pro-inflammatory cytokine; Antioxidant enzymes.

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1. INTRODUCTION

Inflammatory bowel disease (IBD) is considered a chronic recurrent inflammatory disorder characterized by development of intestinal inflammation resulting from the transmural infiltration of neutrophils, macrophages, lymphocytes and mast cells, ultimately giving rise to mucosal disruption and ulceration, it refers essentially to 2 chronic intestinal disorders: Crohn's disease (CD) and ulcerative colitis (UC) (Abraham and Cho, 2009). Ulcerative colitis is a chronic and non-specific inflammatory disorder primarily involving the mucosa and sub-mucosa of the colon, whose etiology is

still unclear (De hertogh et al., 2008). UC characterized by rectal bleeding and diarrhea resulting in disruption of the epithelial barrier, and the formation of epithelial ulceration (Silva et al., 2010).

A model of acute colitis in animals has been achieved by the intrarectal administration of toxic agents such as 2, 4, 6-trinitrobenzenesulfonic acid (TNBS) into rat colon (Nieto et al., 1998). This model resembles many of the clinical, histological features of the human UC such as transmural inflammation with granuloma and Langhans-type giant cells, skip segment ulceration and inflammation, cobble stone like appearance of the mucosa. Infiltrated granulocytes and macrophages produce high levels of pro-inflammatory cytokines, such as TNF-α, clearly involved in the pathogenesis of IBD. Among immune mediators, mast cells may play an important role in the recovery of the intestinal dysfunction, and although its involvement is still little understood, different proteases and other cellular products liberated in function of their considerable heterogeneity could play a key role, especially in more advanced states of the reparative process (Santos et al., 2005).

Trinitrobenzenesulfonic acid may be metabolized, enzymatically or non-enzymatically by ascorbate to yield superoxide anion (O^{-}_{2}) (Grisham et al., 1991), and hydrogen peroxide (H_2O_2), suggesting that TNBS-induced colitis may be partially mediated by cytotoxic reactive oxygen metabolites generated by the oxidative metabolism of TNBS (Kunin and Gallily, 1983).

Rutin (a quercetin-rhamnoglucoside) is a glycosylated conjugate of quercetin (quercetin- 3-rutinoside) is one of the most common native flavonoids occurring mainly in glycosidic forms (Kamalakkannan and Prince, 2006). Also, it is a powerful antioxidant (La-Casa et al., 2000) with anti-inflammatory activity (Han, 2009). Moreover, a series of complexes of this ligand display an enhancement of free radical scavenger ability (Kostyuk et al., 2007).

Accordingly, the purpose of the present study was to investigate the effect of rutin against TNBS induced colitis in rats. Also, to determine whether rutin when administered to ulcerative colitis induced-rats would attenuate the oxidative stress in colon tissue, beneficial for prevention and treatment of colitis complications.

2. MATERIALS AND METHODS

2.1. Experimental animals:

Fourty white male albino rats of 12-16 weeks old and weighting 180-220 gm were used in the experimental investigation of this study. The rats were obtained from the Laboratory Animals Research Center, Faculty of Veterinary Medicine, Benha University. Rats were housed in separated wire mesh cages and kept at constant environmental and nutritional conditions throughout the period of experiment. The animals were fed on constant ration and fresh, clean drinking water was supplied ad- libitum. The animals were left 14 days for acclimatization before the beginning of the experiment.

2.2. Rutin:

Rutin is pale yellow crystalline powder (purity~99%). It was purchased from EPICO 'Egyption Pharmaceutical Industries Company, 10th of Ramadan city, Egypt. Rutin was dissolved with in propylene glycol solution and administered to rats in daily oral dose of 200 mg/kg body weight for 21 days (Abdel-Raheem, 2010).

2.3. Induction of colitis:

To induce colitis, rats were fasted for 36 hours, and then anaesthetized with an i.p. injection of sodium thiopental (500 mg dissolved in 12.5 ml of normal saline) at the dose level of 0.2 ml/200gm body weight (40 mg/kg bw i.p.) (Motavallian et al., 2012).

TNBS was then administered intra-colonially of rats (150mg/kg b.wt) (Jun-Hua Li et al., 2005), in a volume of 0.5ml, via a polyethylene catheter inserted 8 cm proximal to the anus (Morris et al., 1989). Rats were positioned head-down for 2-3 minutes to preclude immediate anal leakage of the instillate and thereafter returned to their cages with access to food and water ad- libitum.

2.4. Experimental design:

Rats were randomly divided into four main equal groups, 10 rats each, placed in individual cages and classified as follow:-
Group 1: Control Normal group: received no drugs, served as control non-treated for all experimental groups.

Group 2: Ulcerative colitis- induced group: Included 10 rats, and served as TNBS-induced colitis groups. This group was divided into two subgroups:

Subgroup (a): consisted of 5 rats, served as colitis non-treated group for comparison with rutin protective group. The experimental UC were induced in rats by TNBS at 20th day from experiment, and the rats were sacrificed 24 hour later of TNBS administration.

Subgroup (b): contain of 5 rats, served as colitis non-treated group for comparison with rutin treatment group. The experimental UC were induced in rats by TNBS at first day of experiment, and the rats were sacrificed after 21 days from induction.

Group 3: ulcerative colitis + RUT protected group: Rats received RUT (200 mg/kg body weight/day) orally for 21 days prior TNBS administration. 24 hour after the administration of TNBS the animals were sacrificed.

Group 4: ulcerative colitis + RUT treated group: The UC in the rats were induced by TNBS at the first day of experiment, after 24 hours rutin treatment (200 mg/kg body weight/day) orally will be started for 21 days, then the animals were sacrificed at 22th day of the experiment.

2.5. Sampling:

Blood samples and tissue specimens (colonic tissues) were collected at the end of experiment on 22th day for all groups (control and experimental groups).

2.5.1. Blood samples:

Blood samples for serum separation were collected by ocular vein puncture at the end of each experimental period in dry, clean, and screw capped tubes and serum were separated by centrifugation at 2500 r.p.m for 15 minutes .The clean, clear serum was separated by automatic pipette and received in dry sterile samples tube and kept in a deep freeze at -20oC until used for subsequent biochemical analysis .All sera were analyzed for Nitric oxide (NO), Tumor necrosis factor-alpha (TNF-α) and Interleukin-1β (IL-1β) determination.

2.5.2. Tissue samples (colon tissue):

At the end of the experiment, rats of each group were sacrificed by cervical decapitation. The abdomen was opened and the colon specimen was quickly removed and opened gently using a scrapper, cleaned by rinsing with ice-cold isotonic saline to remove any blood cells, clots and scraps of food, then blotted between 2 filter papers and quickly stored in a deep freezer at (-20 °C) for subsequent biochemical analysis. Briefly, colon tissues were divided into appropriate portions, homogenized with a glass homogenizer in 9 volume of ice-cold 0.05 mM potassium phosphate buffer (pH7.4) to make 10% homogenates. The homogenates were centrifuged at 6000 r.p.m for 15 minutes at 4°C then the resultant supernatant were used for the determination of the following parameters: GPx, CAT, SOD, GST, GR, GSH, L-MDA and MPO.

2.6. Biochemical analysis:

Serum NO, TNF-α and IL-1β and colon tissue GPx, SOD, CAT, GST, GR, GSH, L-MDA and MPO activity were analyzed according to the methods described by Vodovotz, (1996); Beyaert and Fiers, (1998); Rat IL-1 beta ELISA (RayBiotech, Inc Company, Cat#: ELR-IL1b); Gross et al., (1967); Kakkar et al., (1984); Luck, (1974); Habig et al., (1974); David and Richard, (1983); Beutler et al., (1963); Mesbah et al., (2004) and Rats Myeloperoxidase ELISA kit (Kamiya Biomedical Company, Cat .No.KT-60345) respectively.

2. 7. Statistical analysis:

The obtained data were statistically analyzed by one-way analysis of variance (ANOVA) followed by the Duncan multiple test. All analyses were performed using the statistical package for social science (SPSS, 13.0 software, 2009). Values of $P<0.05$ were considered to be significant.

3. RESULTS

3.1. Effect of pretreatment with rutin on some serum and colon tissue parameters of TNBS-induced ulcerative colitis in rats.

The obtained results in table (1) revealed that, a significant decrease in serum NO level and GST, CAT, SOD and GPx activities in colon tissue were observed in TNBS induced UC in rats. On the other hand, a significant increase in serum TNF-α and IL-1β concentrations and colon tissue MPO, L-MDA and GSH accompanied with a non-significant increase in GR activity were observed in UC induced rats. Pretreatment with RUT in TNBS-induced ulcerative colitis in rats resulted in significant increase in serum NO level and GST, CAT, SOD and GPx activities in colon tissue. Meanwhile, a significant decrease in serum TNF- α and IL-1β concentrations and colon tissue MPO, L-MDA, GSH and GR were significantly decreased when compared with UC non treated group.

3.2. Effect of rutin treatment on some serum and colon tissue parameters of TNBS-induced ulcerative colitis in rats.

The obtained results presented in table (2) revealed that, a significant decrease in serum No, colon tissue GST, CAT, SOD and GPx activities were observed in UC induced rats. On the other hand, a significant increase in serum TNF-α and IL-1β concentrations and colon tissue MPO, L-MDA, GSH and GR were observed in UC induced rats when compared with control group. Treatment with RUT in TNBS-induced ulcerative colitis in rats resulted in significant increase in serum NO level and colon tissue GST, CAT, SOD and GPx activities. Meanwhile, the value of serum TNF-α and IL-1β and colon tissue MPO, L-MDA, GSH were significantly decreased accompanied with a non-significant decrease in GR activity as compared with UC non treated group.

4. DISCUSSION

Mouse models of inflammatory colitis such as dextran sulfate sodium (DSS)-induced and TNBS-induced colitis have been used to study various aspects of acute and chronic inflammation as well as mechanisms involved in colonic healing. Rectal administration of TNBS dissolved in ethanol initiates a severe inflammatory response and usually transmural tissue necrosis that can be followed by regeneration (Elson et al., 1995).

Table (1): Effect of pretreatment with rutin on some serum and colon tissue parameters of TNBS-induced ulcerative colitis in rats.

Parameters	Experimental groups at Protective period		
	Control Normal group	TNBS induced UC group	TNBS + RUT protected group
NO (mmol/L)	81.57 ± 3.61 [a]	41.08 ± 3.31[b]	88.15 ± 3.44 [a]
TNF- α (pg/ml)	22.53 ± 3.65 [d]	75.39 ± 5.60 [a]	53.28 ± 4.21 [b]
IL- 1β (pg/ml)	173.11 ±25.07 [d]	694.76 ± 31.57 [a]	492.93 ± 20.67 [b]
L-MAD (mmol/g.tissue)	45.37 ± 8.56 [c]	163.44 ± 11.18 [a]	119.14 ± 9.79 [b]
MPO (ng/g.tissue)	3.64 ± 0.47 [c]	15.32 ± 1.10 [a]	11.60 ± 0.98 [b]
GPx (ng/ g.tissue)	32.33 ± 4.66 [a]	9.06 ± 1.82 [c]	19.86 ± 2.39 [b]
SOD (U/g.tissue)	27.57 ± 3.05 [ab]	11.82 ± 1.94 [c]	27.06 ± 1.59 [ab]
CAT(mmol/g.tissue)	63.70 ± 4.22 [a]	17.12 ± 3.74 [c]	51.43 ± 2.72 [b]
GST (ng/g.tissue)	0.57 ± 0.04 [a]	0.22 ± 0.03 [c]	0.35 ± 0.02 [b]
GR (ng/g.tissue)	2.25 ± 0.22 [ab]	2.74 ± 0.25 [a]	1.92 ± 0.10 [b]
GSH (ng/g.tissue)	2.92 ± 0.46 [c]	8.79 ± 1.37 [a]	5.29 ± 0.62 [bc]

Data are presented as (Mean ± S.E). S.E = Standard error.
Mean values with different superscript letters in the same row are significantly different at ($P<0.05$).

Table (2): Effect of rutin treatment on some serum and colon tissue parameters of TNBS-induced ulcerative colitis in rats.

Parameters	Experimental groups at treatment period		
	Control Normal group	TNBS induced UC group	TNBS + RUT treated group
NO (mmol/L)	81.57 ± 3.61 [a]	61.78 ± 4.64 [d]	97.53 ± 6.32 [ab]
TNF- α (pg/ml)	22.53 ± 3.65 [d]	60.04 ± 3.13 [a]	26.68 ± 2.77 [bc]
IL- 1β (pg/ml)	173.11 ±25.07 [d]	675.58 ± 48.43 [a]	252.44 ± 16.69 [bc]
L-MAD (mmol/g.tissue)	45.37 ± 8.56 [c]	168.60 ± 20.56 [a]	82.94 ± 4.73 [b]
MPO (ng/g.tissue)	3.64 ± 0.47 [c]	12.16 ± 0.51 [a]	7.41 ± 0.96 [b]
GPx (ng/ g.tissue)	32.33 ± 4.66 [a]	10.39 ± 1.65 [b]	25.89 ± 2.13 [a]
SOD (U/g.tissue)	27.57 ± 3.05 [ab]	15.11 ± 2.16 [b]	30.21 ± 1.59 [a]
CAT(mmol/g.tissue)	63.70 ± 4.22 [a]	18.31 ± 4.28 [c]	56.72 ± 6.88 [ab]
GST (ng/g.tissue)	0.57 ± 0.04 [a]	0.21 ± 0.04 [c]	0.47 ± 0.04 [ab]
GR (ng/g.tissue)	2.25 ± 0.22 [ab]	3.04 ± 0.29 [a]	2.45 ± 0.07 [ab]
GSH (ng/g.tissue)	2.92 ± 0.46 [c]	8.39 ± 1.11 [a]	2.29 ± 0.55 [b]

Data are presented as (Mean ± S.E). S.E = Standard error.
Mean values with different superscript letters in the same row are significantly different at ($P<0.05$).

The obtained data presented in tables (1 and 2) revealed that, a significant decrease in serum NO. Inhibition of NO synthesis has been found to increase acute damage of the intestinal mucosal from immune-mediated stress, such as ischemia– reperfusion and septic injury (Kubes, 1993). Administration of rutin in TNBS-induced ulcerative colitis in rats resulted in a significant increase in serum NO concentration. Administration of exogenous NO protects the mucosa against the a fore mentioned models, and this protective effect may be exerted at different levels, including maintenance of blood flow, inhibition of platelet and leucocyte adhesion and ⁄or aggregation within the vasculature, down-regulation of mast cell reactivity, and modulation of oxidative stress, resulting in the inhibition of nuclear factor-kB (NF-kB) translocation (Alican and Kubes, 1996). In addition, NO can reduce superoxide induced damage either by inhibiting NADPH oxidase and superoxide release from neutrophils, or by scavenging neutrophil-derived superoxide (Clancy et al., 1992). Accordingly, NO donors have been found to double the plasma antioxidant capacity of animals subjected to reperfusion-induced mucosal injury. Considering the above observations, it would seem logical that the production of large quantities of NO, even iNOS derived, would improve blood flow, reduce leucocyte and platelet recruitment and oxidative stress, and hence reduce inflammation.

The obtained data presented in (Tables 1and 2) revealed that, a significant increase in serum TNF-α and IL-1β concentrations were observed in TNBS induced UC in rats. These results are nearly similar to those reported by Xin and Jianming, (2011) who demonstrated that, the levels of TNF-α in TNBS model group showed a significantly high expression compared with normal control group. Colonic administration of TNBS was shown to increase the production of serum IL-1β and colonic NF-kappa-B, which were found to be associated with increases in colonic damage score (Song et al., 2006). In the present study, the increased tissue levels of the pro-inflammatory cytokines TNF-α, IL-1β and IL-6 by colitis induction also support the notion that tissue injury induced by TNBS involves the enhanced generation of inflammatory cytokines.

Rutin treatment in TNBS induced UC in rats significantly decreased serum TNF-α and IL-1β concentrations. TNF-α and IL-6 are multifunctional cytokines produced primarily by activated monocytes and macrophages; they play a crucial role in the initiation and continuation of mucosal inflammation and immunity (Tracey and Cerami, 1994). These cytokines are involved in many cell processes including apoptotic cell death, metabolism, inflammation, thrombosis and fibrinolysis (Nilsen et al., 1998). TNF-α and IL-6 induce the production of other cytokines including adhesion molecules and arachidonic acid metabolites, and activation of immune and non-immune cells (Bobin-Dubigeon et al., 2001). Moreover, Worledge et al., (2000) reported that the administration of TNF-α antibodies effectively treated experimental colitis in rats. In the present study, TNF-α and IL-1β levels were correlated with the increased level of inflammation in the colitis group. By contrast, TNF-α and IL-1β levels decreased in all study groups, this decrease was more significant in the rutin treated groups. At this point, TNF-α and IL-1β may be promising markers in monitoring the progress of IBD and the response to treatment.

The obtained results in (Tables 1, 2) showed a significant decrease in colon tissue GST, CAT, SOD and GPx activities in TNBS induced UC in rats. On the other hand, a marked increase in colon tissue GSH and L-MDA concentrations, MPO and GR activities were observed in UC induced group. These results are nearly similar to those recorded by Xing et al., (2012) who reported that, SOD

and GPx activities and GSH levels were decreased in colon tissues and serum of experimental colitis in rats after induced by TNBS.

The tissue Myeloperoxidase (MPO) and Malondialdehyde (MDA) levels were used as biomarkers for inflammation oxidative stress in TNBS administered group, respectively. Infiltration of leukocytes into the mucosa has been suggested to contribute significantly to the tissue necrosis and mucosal dysfunction associated with colitis as they represent a major source of reactive O^2 radicals in the inflamed mucosa. These reactive oxygen species degrade polyunsaturated lipids, forming malondialdehyde. This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form advanced glycation end products. The production of this aldehyde is used as a biomarker to measure the level of oxidative stress (Hagar et al., 2007). Thus, increased colonic tissue level of MDA is used as one of the parameters to study the tissue damage via lipid peroxidation. This inhibition of the generation of malondialdehyde and lipid peroxidation may possibly help to decrease the tissue damage.

Chronic inflammation of the large intestine predominantly comprises lymphocytes and plasma cells exacerbation, neutrophils migrate and degranulate substances like MPO. It is an enzyme found in primary granules of polymorph nuclear neutrophils and used as an index for the severity of digestive inflammation (Masoodi et al., 2011). Myeloperoxidase is secreted by the neutrophils whenever there is inflammation and therefore the number of neutrophils is directly co-related with myeloperoxidase activity. Neutrophils play an important role in producing superoxide anion and a cascade of various reactive species leading to a very reactive hydroxyl and peroxide radicals (Zheng et al., 2000). In fact, it is well-known that this enzyme is increased in TNBS and DSS- induced colitis (De-Faria et al., 2012).

Oxidative stress is known to play an important role in IBD initiation and progression (Kruidenier and Verspaget, 2002). Experimentally induced colitis in animals is characterized by oxidative damage and an imbalance between oxidant and antioxidant substances (Dröge, 2002). Several studies have indicated the vital role that free radicals play in the pathogenesis of mucosal injuries (Isozaki et al., 2006). Moreover, free radicals and ROS were reported in colorectal specimens of ulcerative colitis (Bitiren et al., 2010). The first line of oxidative defense system against free radicals is the sulphadryls groups in peptide namely GSH. It is widely distributed in all biological tissues and work as a non-enzymatic antioxidant. GSH inhibits ROS oxidative injuries directly *via* its sulfhydryl group and indirectly as a cofactor or a coenzyme in ROS enzymatic detoxification process (Sivaprasad et al., 2004). Another line in oxidative defense system is the enzymatic antioxidants. Examples for important antioxidant enzymes are SOD, CAT, and GPx (Boots et al., 2008). In present study, activities of enzymatic defense systems were severely decreased in the colon tissue of TNBS administered animals indicating oxidative cellular injury. Furthermore, free radicals are known to attack lipid contents of cellular membranes leading to activation of LPO process and cellular damage.

The increase in glutathione appears to result in efficient glutathione recycling. Although the increase in the activity of GR can promote the recycling of glutathione for the active detoxification of xenobiotics and the decrease in GPx activity may attenuate the radical scavenging function (Oh et al., 1998). GR accelerating the conversion of GSSG to GSH and enhancing the detoxification of

reactive metabolites by conjugation with GSH (Panda et al., 2012).

Administration of rutin in TNBS-induced ulcerative colitis in rats resulted in significant increase in colon tissue GST, CAT, SOD and GPx activities. Meanwhile, colon tissue MPO, L-MDA, GSH and GR activity were significantly decreased. Free radicals react with lipids in cell membranes and form lipid peroxides and this changes the integrity of cells. Rutin, being an anti-lipoperoxidant agent, inhibits formation of lipid peroxides (Nègre-Salvayre et al., 1991). Recent study on two bioflavonoids, rutin and qurecetin, showed they decreased MDA levels and increased antioxidant enzyme levels in cardiac ischemia reperfusion injury. The mechanism of reperfusion injury induced oxidative stress is similar in cardiac reperfusion injury and testicular ischemia reperfusion injury (Annapurna et al., 2009).

Rutin treatment significantly improves the activity of GPx, SOD and catalase thus suggesting its role in scavenging the free radicals generated by TNBS. Also, the significant decrease in MDA level that may be due to the acute antioxidant effects of the bioflavonoid rutin that showed maximum benefits, higher scavenger efficiency and more antioxidant activity, which seems to be correlated to its structure (Akondi et al., 2011). This effect may be attributable to the catechol structure of ring B, the 2, 3 double bond in conjugation with a 4-oxo function, and the presence of both 7- and 5-hydroxyl groups (Russo et al., 2000). Rutin is a well-known scavenger of ROS such as superoxide anions, hydroxyl radicals, and peroxynitrite anion. Wei et al., (2011) showed that, rutin treatment significantly improved superoxide dismutase and catalase activities in ipsilateral testes. These results suggest that rutin may scavenge ROS by enhancing the activities of these antioxidant enzymes in testes (Jeong et al., 2009).

Rutin treatment significantly reduced the inflammation characterized by decrease in myeloperoxidase activity. Quercetin and rutin have been shown to have inhibitory effect on myeloperoxidase (MPO) activity in vitro. Quercetin directly scavenges hypochlorous acid (HOCl), a chlorinated species generated by the $MPO/H_2O_2/Cl^-$ system (Pincemail et al., 1988). The MPO/nitrite-mediated lipid peroxidation of LDL was effectively blocked by the quercetin and rutin (Kostyuk et al., 2003).

In conclusion, the present study demonstrated that rutin administration provided an effective protection against colitis and oxidative damage in colon mucosal tissue induced by TNBS in rats, since rutin was able to ameliorate serum biochemical parameters, enzymatic and non-enzymatic antioxidant defense system in colon mucosa tissue. We recommended that, administration of diet rich in the antioxidant flavonoid is very important for protection of different body tissue, especially colon tissue, against oxidative stress or even inflammation or erosion.

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التأثيرالمضاد للألتهابات والأكسدة للروتين على التهاب القولون التقرحي المحدث بحمض تراي نيتروبنزين سلفونيك في الفئران

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الملخص العربي

في هذه الدراسة تم تقييم التأثير الوقائي والعلاجي للروتين على التغيرات في مستوى أكسيد النيتريك، عامل التنخر الورمي الفا، والأنترلوكين 1- بيتا. بالإضافة الى الأكسدة الفوقية للدهون، مضادات الأكسدة الأنزيمية والغير انزيمية، نشاط الميلوبيروكسيديز في دم وأنسجة الجرذان المستحدث فيها التهاب القولون التقرحي بحمض تراي نيتروبنزين سلفونيك. هذا وقد أستخدم لأجراء هذه الدراسة عدد 40 من ذكور الجرذان البيضاء أعمارهم تتراوح من 12-16 أسبوع و أوزانها من180 - 250جرام وقد قسمت إلى أربع مجموعات متساوية اشتملت كل مجموعة على عدد عشرة فئران وتم توزيعها كالآتي: المجموعة الأولى: (المجموعة الضابطة): لم تعطى أي أدوية واستخدمت كمجموعة ضابطة للمجموعات الأخرى. المجموعة الثانية: (المجموعة المحدث بها مرض التهاب القولون التقرحي): تم اعطاء حمض تراي نيتروبنزين سلفونيك عن طريق القسطرة في القولون بتركيز 150 مللي جرام/كيلوجرام لأحداث التهاب القولون التقرحي. المجموعة الثالثة:(المجموعة الوقائية بالروتين ومصحوبة بالتهاب القولون التقرحي): تم تجريع الفئران بالروتين لمدة 21 يوم يومياً عن طريق الفم بجرعة مقدراها (200 مللى جرام/ كيلوجرام) ثم تم حقنها بحمض تراي نيتروبنزين سلفونيك لأحداث التهاب القولون التقرحي. المجموعة الرابعة:(المجموعة المعالجة بالروتين بعد احداث التهاب القولون التقرحي): تم حقن الفئران بحمض تراي نيترو بنزين سلفونيك لأحداث التهاب القولون التقرحي ، بعد 24 ساعة تم بدء العلاج بالروتين بتجريع الفئران لمدة 21 يوم عن طريق الفم بجرعة مقدراها (200 مللى جرام/ كيلوجرام). وقد تم تجميع عينات الدم والأنسجة فى اليوم الثاني والعشرون من بدايه التجربة. وقد أسفرت نتائج التحليل البيوكيميائى عن وجود انخفاض معنوى فى كلا من أكسيد النيتريك، نشاط الجلوتاثايون بيروكسيديز، سوبر أكسيد ديسميوتيز، الكتاليز، الجلوتاثايون-اس-ترانسفيريز في نسيج القولون، من جهة اخرى اظهرت النتائج زيادة في انزيم الجلوتاثايون ريدكتاز، ريديوسيدجلوتاثايون، ال - مالونديالدهيد، عامل التنخر الورمي – الفا والأنترلوكين1 - بيتا فى المجموعه المحدث بها التهاب القولون التقرحي. كما أن نتائج مجاميع الجرذان المحدث بها مرض التهاب القولون التقرحي والتي تم وقايتها وعلاجها بالروتين أظهرت زيادة في كلا من أكسيد النيتريك، نشاط الجلوتاثايون بيروكسيديز، سوبر أكسيد ديسميوتيز، الكتاليز، الجلوتاثايون-اس-ترانسفيريز في نسيج القولون، من جهة اخرى اظهرت النتائج البيوكيميائية الحيوية للروتين زيادة في انزيم الجلوتاثايون ريدكتاز، ريديوسيدجلوتاثايون، ال - مالونديالدهيد، عامل التنخر الورمي – الفا والأنترلوكين1 - بيتا فى المجموعة المحدث بها التهاب القولون التقرحي. وأوضحت الدراسة أن استخدام الروتين كماده واقية مضادة للأكسدة ومضادة للالتهابات كان لها دور فعال في حماية الغشاء المبطن للقولون من التنكرز والتقرح المحدث تجريبيا فى الجرذان باستخدام حمض تراي نيترو بنزين سلفونيك و أدى استخدامه كذلك الى الحفاظ على نسب القياسات البيوكيميائية فى الدم والأنسجة لما يقارب النسب الطبيعية. لذلك توصى الدراسة بضرورة استغلال تلك المزايا الهائلة للروتين كماده وقائية وعلاجية و مضادة للأكسدة والالتهابات و إدخاله كماده فعالة فى صناعة العقاقير الطبية المستخدمة فى وقاية و علاج القولون من الالتهابات والقرح.

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