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Original article

Ameliorative effects of ribes rubrum oil against gastric ulcers caused by indomethacin in experimental models

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ABSTRACT

The objective of this study was to assess the anti-inflammatory effects of ribes rubrum oil at three different doses (5, 10 and 15 ml/kg b.w/day) in adult male albino rats with indomethacin-induced stomach ulcers (IND). Forty rats (135 ± 5 g) categorized into 5 groups (n = 8), for 45 days. Group (1) normal control, thirty-two rats were gavaged IND as single oral dose (30 mg/Kg b.w) resulted in gastric ulcer, then distributed to four groups, group (2) IND-intoxicated control, Groups 3, 4 and 5 were administrated ribes rubrum oil at levels of (5, 10 & 15 ml/kg b.w) respectively. Administrated levels of ribes rubrum oil found to have remarkable elevation in food conversion efficiency in experimental rats, gastric juice pH, in compared to the drunken control group, gastric prostaglandin E2 and gastric cytochrome P450 reductase levels were lower. The levels of pro-inflammatory cytokines NO, TNF-, and IL-1 were dramatically reduced, which was related with an increase in blood hemoglobin (Hb), packed cell volume (PCV), and red blood cells (RBCs)in ulcerogenic rats compared to intoxicated control. Data showed that, the main components of ribes rubrum oil are β-Pinene, γ-linolenic and Linalool oxide levels (25.9%, 23.10% and 10.5%, respectively) for their antioxidant activity. Findings showed that administrate ribes rubrum oil at dose 15 ml/kg followed by 10 ml/kg had the best results against ulcerogenic rats. In conclusion, the outcomes are consistent with the concept that ribes rubrum oil had a gastroprotective and antisecretory effects against gastric ulcer that may be attributed to the antioxidant properties of the oil that ameliorates the damage occur in gastric of rats.

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1. Introduction

One of the most common gastrointestinal tract pathogens is gastric ulcer that harmed humans for centuries. Exogenous factors that because peptic ulcers include the use of nonsteroidal anti-inflammatory medicines (NSAIDs), anxiety, nutritional inadequacies, smoking, and a hereditary propensity. In addition to intrinsic variables such as gastric acid, pepsin exudation, gastric microcirculation, prostaglandin E2 (PGE2) content, and interleukin (IL)-1 release, all of which play a significant role in the course of gastric mucosal injury (Wang et al., 2011).

Non-steroidal anti-inflammatory medicines are used as costly financial burdens throughout the world. Indomethacin is an anti-inflammatory non-steroid that reduces fever, pain and inflammation. It works by reducing the production of prostaglandins like ibuprofen and naproxen (Takeuchi et al., 1991). Indomethacin prevents and reduced prostaglandin levels in enzymes producing prostaglandins (COX1 and COX 2). The result is reduced fever, pain and swelling. Indomethacin in an extended release form is available (De La Lastra et al., 2002). Nowadays, gastric ulcer therapy is severely hampered because the vast majority of drugs on the market today have low efficiency against gastric disease and frequently have severe side effects.

Herbal medicines are in constant expansion globally for the prevention and treatment of diverse illnesses. In the Gooseberry family Grossulariaceae, Ribes rubrum (*Ribes rubrum* L.) is a part of a genus of Ribes. Ribes rubrum is a good source of anthocyanins. A diverse range of phenolics also contains high antioxidant levels and major polyunsaturated acids with pungent constituents, such as α-linolenic acid and μ-linolenic acid, that are distinguishable among plants oils, in particular ascorbial acid and minerals, in particular potassium, calcium and magnesium. Polyunsaturated fatty

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acids are quickly affected to oxidation, but somehow, they are stabilized in the intact seeds, suggesting existence of powerful natural antioxidants, that makes ribes rubrum an interesting target of functional foods (Leskinen et al., 2009; Nour et al., 2011). Furthermore, extracts of ribes seed exert health effects to many diseases, with many biological actions that attributed to their antioxidant activity (Gođevac et al., 2012). As a source of gamma-linols and tocopherols, rib oils offer significant promise, and contain relatively large concentrations of these chemicals. Gamma linolenic acid is a vital human component since it intermediates chemicals such as prostaglandins, prostacyclin and thromboxane for biosynthesis (Fan and Chapkin, 1998; Goffman and Galletti, 2001). Numerous researches have shown that gamma linolenic acid acts as a strong scavenger and has several health benefits. The effects are anti-inflammable and antiproliferative, decrease body fat and facilitate beta-oxidation of fatty acids in the liver (Aneta et al., 2013; Takada et al., 1994), it works as a powerful cytotoxic agent for superficial gallbladder cancer (Makarova and Eremeeva, 2015; Solomon et al., 1998). Medicinal plant intervention entails financial strain and has an uncertain reported incidence (Okewumi and Oyeyemi, 2012). The present investigation was therefore conceived to hypothesize the potential protective impact of rubber rib natural oil on gastrical mucosal injury caused by indomethcin to rats.

2. Material and methods

Plant material: Agricultural Research Centre, Giza, Egypt, was the source of ribes rubrum oil for conducting this study.

Experimental animals: Forty male albino rats of the Wistar breed weighing 1255 g were acquired from Animal Colony in Helwan, Egypt. The animals were fed a formulated food and water ad libitum for seven days prior to the trial, according to NRC (Council, 1995), and were monitored.

Drugs: Indomethacin (IND) was obtained from SEDICO Pharmaceutical Company, Giza, Egypt.

2.1. Methods

DPPH Radicals Scavenging activities: The Ribes rubrum oil antioxidant activity was measured using the DPPH assay (Malenčić et al., 2007).

GC–MS (Gas Chromatography–Mass Spectrometry): Oil of Ribes rubrum were analyzed according to Adams et al studies with slight modification (Adams, 2001). The GC equipment was an Agilent technology (HP) 6890 system with an HP-5MS (60 m 0.25 mm, film span 0.25 ml) capillary column. The program began with the oven temperature at 40 °C, which was maintained for 1 min before being increased to 230 °C at a rate of 3C/min and maintained for 10 min. Helium was used as a carrier gas at a flow rate of 1.0 ml/min. The detector and injector had temperatures of 250 and 280 °C, respectively. The HP 6890 GC analysis was performed on the same capillary column as previously on a 5973-network mass selector detector with carrier gaseous helium at a rate of one ml/min and a split rate of 1/50. The petroleum compounds were identified by comparing their retention indices (RI), mass spectrum fragmentation to those found in the Wiley 7n.1 mass computer library, NIST (National Institute of Standards and Technology).

Indomethacin-induced gastric ulcer: According to Sayanti *et al* a single indomethacin dose (30 mg/kg body weight) was given to rats to create stomach damage (Bhattacharya et al., 2007).

Experimental procedures: All rats were fed a baseline diet for one week prior to the start of the experiment, then the forty rats categorized into 5 groups (n = 8), for 45 days. Group (1) normal control, the rest thirty-two rats were gavaged IND as single oral dose (30 mg/kg b.w) resulted in gastric ulcer, then distributed to four groups, group (2) IND-intoxicated control, Groups 3, 4 and 5 were administrated ribes rubrum oil at levels of (5, 10 & 15 ml/kg b.w) respectively, orally by stomach tube. Weekly food intake and weight growth were calculated. The food efficiency ratio (FER) was developed in accordance with the plan of (Chapman et al., 1959). The experimental methodology was followed in compliance with European Community Directive 2010/63/EU. After fasting overnight, after ether anesthesia, rats were slaughtered at the end of the experiment. The blood samples have been obtained from the vein of the hepatic portal, a little portion of the tube has been extracted and the remaining parts left at room temperature to clot for 15 min then centrifuged for 20 min at 3000 rpm. Serum has been properly separated and transformed into clean plastic pipes which have been fairly fit and frozen at −20 °C until the analysis is complete.

Determination of Gastric Ulceration: With a minor nick, the stomach fundus was drilled at a higher stomach curvature. The larger stomach curvature was opened and injected with the cardiac and pyloric end ligation by distilling water (3 ml). It was collected and measured the volume and pH of the accumulated stomach fluid. In the ulcer index calculations, gastric mucosa was found under the lupus glass (Kiliç et al., 2006). Ulcer index (UI) and curative ratio were recorded along with (Parmar and Desai, 1993) by the formula:

UI = 1 × (number of lesions of grade 1) + 2 × (number of lesions of grade 2) + 3 × (number of lesions of grade 3). Then a factor of 10 divided the overall result, which was identified as an index of the ulcer. Also, the curative ratio was recorded for each group as following:

"Curative ratio = (length of gastric ulcer in control positive group − length of gastric ulcer in treated group / length of gastric ulcer in control positive group) × 100".

2.2. Biochemical analysis

Analyses of blood parameters: Hemoglobin, packed cell volume and Red blood cells (RBCs) were estimated respectively (Cynthia et al., 1993;Drabkin, 1949;MC-INORY, 1954). The serum was collected from the left blood after coagulated and centrifuged for 15 min at 3000 rpm. Nitric oxide (NO), interleukin 1 (IL-1ß), and tumor necrosis factor alpha (TNF-α) levels were all measured (Beutler et al., 1985; Grassi et al., 1991; Green et al., 1982).

Gastric mucosa determination: The gastric mucosa was determined in accordance with the criteria for cyclooxygenase gastric (cox-2) cytochromes; prostaglandin E2 (PGE2), cytochrome P450 reductase (cytopotamina-450) (Hamberg and Samuelsson, 1973; Hemler and Lands, 1976; McLean and Day, 1974).

Statistical analysis: The results were explored in one-way analyze of variance followed by the Multiple Range Test by Duncan using version 11 of SPSS (SPSS, Chicago, IL) (DMRT) (Snedecor and Cochran, 1969). The $P < 0.05$ was chosen for statistical meaning (Khan et al., 2019).

3. Results

GC–MS profiling of oil of ribes rubrum revealed the presence of 6 different phytoconstituents consisting of β-Pinene (25.9%), followed by γ-linolenic (23.10%), Linalool oxide (10.5%), 1,8-Cineol (4.6%), α–Epi bisabolol (3.55%) and Myristicin (2.17%) respectively (Table 1). The statistical data in Table 3 predicted that, intoxicated rat group showed decline in food conversion efficiency in IND administrated intoxicated group, while treated with (5, 10 and 15 ml) ribes rubrum oil showed no significant difference in final weight, weight gain, food intake and FER comparing with normal control. The presented data in Table 4 indicated that indomethacin

Table 1
Chromatography analysis of ribes rubrum oil (GC/GC–MS).

Component	Content (%)
1,8-Cineol	4.6
β-Pinene	25.9
Linalool oxide	10.5
Myristicin	2.17
α-Epi bisabolol	3.55
γ-linolenic	23.10

Table 2
Antioxidant activity of ribes rubrum oil.

Parameters	Scavenging activity of DPPH radicals (%)
5 (μg/ml)	75.4 ± 1.6
10 (μg/ml)	87.7 ± 1.7
15 (μg/ml)	97.3 ± 2.2*
20 (μg/ml)	93.2 ± 1.5

administration effectively induced ulcer in rats which was confirmed by elevated volume levels of gastric juice allied with momentous reduce in intoxicated rat group PH. On the other hand, treating with ribes rubrum oil with different levels produced a momentous reduces in volume of gastric juice and a noteworthy elevation in PH compared to intoxicated control group. Significant decrease was witnessed on values of gastric ulcer index of all treated rat groups in contrast with intoxicated group. Treating with ribes rubrum oil at doses of (5, 10 and 15 ml) showed no significant difference in curative ratio percentage. On the other hand, the ribes rubrum oil at doses (5, 10 and 15 ml) treated groups showed no significant difference of Hb, PCV and RBCs levels in comparison to normal control (Table 5).

Table 6 reported that the delivery of indomethacin to rats resulted in a significant ($p < 0.05$) decrease in rats' levels of gastric COX-2 and PGE_2 (prostaglandin E2) and momentous increase in cytochrome P_{450} reductase activity (Cyto P_{450}) levels as compared to normal control group (Table 6).

4. Discussion

The most abundant fatty acids in ribes rubrum oil were β-Pinene and γ-linolenic acids, comprising 49% of the total fatty acids. γ-linolenic is a vital fatty acid for human and an intermediary component in the formation of prostaglandins, tromboxanes and prostacyclins (Paccalin et al., 1985). Crucial rib oil fatty acids have been shown to be anti-inflammatory and anticancer (Goffman and Galletti, 2001). Furthermore, several studies demonstrated that γ-Linoleic acid is a powerful antioxidant, having various health benefits, such as reducing body fat and reducing hepatic beta-oxidation in fatty acid, increase muscle and bone strength, boost and strengthen an immune system (Makarova and Eremeeva, 2015; Takada et al., 1994). These results were supported with measuring Antioxidant activity (as DPPH) for Ribes oil that presented in Table 2. DPPH radical scavenging activity of oil assorted from 5 to 20 (μg/ml) with high antioxidant activity for (15 μg/ml) with 97.3% followed by (20 μg/ml) with antioxidant activity 93.2%, (10 μg/ml with 87.7%) and (5 μg/ml with 75.4%). These results are in parallel with the finding of (Velioglu et al., 1998) as they reported that the antioxidant of ribes rubrum was 90.86% with total phenolics 1421(mg GAE/100 g).

This decrease in nutritional parameters may be due to decrease of appetite, disturbance of stomach enzymes' secretions, with alterations in the PH of the gastric secretion addition to neuropeptide-Y hormone levels. These results are in correlation with the findings of previous studies (El-Metwally, 2014; Haithem et al., 2014; Helmy, 2011). Using ribes rubrum oil (RRO) in treatment of ulcer at doses of (5, 10 and 15 ml) resulted in significant elevation in food conversion efficiency compared to intoxicated group. These data may be based on the bioactive characteristics of oil with antioxidant and its pharmaceutical effects on the healing of gastric ulcers (Chiang et al., 2005; Makri and Kintzios, 2008).

Individual mechanisms, like production of reactive oxygen (ROS), commencement of lipid peroxidation and inhibition of prostaglandin synthesis may be ascribed to the ulceration generated by indomethacin. The decreased prostaglandin level undermines nearly every component of gastritis and increases acid discharges

Table 3
Food conversion efficiency in normal and IND administrated groups.

Groups	Normal Control	Intoxicated Control	Treated with RRO		
Variables			5 ml/kg	10 ml/kg	15 ml/kg
Initial weight (g)	120.31 ± 3.45 ^{a}	122.24 ± 4·55 ^{a}	123.21 ± 3.55 ^{a}	121.36 ± 4.77 ^{a}	124.31 ± 5.01 ^{a}
Final weight (g)	236.08 ± 27.17 ^{a}	189.13 ± 17.37^{b**}	226.35 ± 22.53 ^{a}	230.08 ± 20.13 ^{a}	232.31 ± 22.34 ^{a}
Weight gain (g)	115.77 ± 8.11 ^{a}	66.89 ± 6.11^{b**}	103.14 ± 9.13 ^{a}	105.77 ± 9.17 ^{a}	108.14 ± 10.15 ^{a}
Food intake (g/w)	15.32 ± 2.14 ^{a}	13.55 ± 2.55 ^{a}	15.45 ± 2.42 ^{a}	15.71 ± 2.71 ^{a}	15.81 ± 2.14 ^{a}
FER	0.125 ± 0.01 ^{a}	0.082 ± 0.03^{b**}	0.111 ± 0.02 ^{a}	0.112 ± 0.05 ^{a}	0.113 ± 0.01 ^{a}

* Values are expressed as mean ± S.D. n = 8 rats/group.
**Values not sharing a common superscript differ significantly at $p < 0.05$ (DMRT)
FER: Food efficiency ratio, RRO: Ribes Rubrum Oil.

Table 4
pH, volume of gastric secretion, ulcer index and Curative ratio% of normal and IND administrated groups.

Groups	Normal Control	Intoxicated Control	Treated with RRO		
Variables			5 ml/kg	10 ml/kg	15 ml/kg
PH	4.17 ± 0.53 ^{a***}	2.03 ± 0.41^{c}	3.34 ± 0.17^{b}	3.69 ± 0.39^{b}	4.08 ± 0.24^{b}
Volume of gastric juice (1 ml)	2.14 ± 0.08^{b**}	5.05 ± 0.16 $_{a***}$	1.53 ± 0.16^{c}	1.87 ± 0.25^{c}	2.07 ± 0.14^{b}
Ulcer index (mm)	–	7.93 ± 0.94 ^{a***}	2.18 ± 0.14^{c}	2.37 ± 0.38^{b}	3.57 ± 0.47^{b}
Curative ratio%	–	–	54.13 ± 4.16 ^{a}	68.44 ± 6.89 ^{a}	75.25 ± 2.47 ^{a}

* Values are expressed as mean ± S.D. n = 8 rats/group.
**Values not sharing a common superscript differ significantly at $p < 0.05$ (DMRT).

Table 5
Hemoglobin (HB), packed cell (PCV) and Red blood cells (RBCs) of normal and IND administrated groups.

Groups	Normal Control	Intoxicated Control	Treated with RRO		
Variables			5 ml/kg	10 ml/kg	15 ml/kg
HB(g/dl)	14.41 ± 1.99[a]	10.53 ± 1.47[b] *	12.97 ± 1.41[a]	13.09 ± 1.44[a]	13.21 ± 1.33[a]
PCV	40.11 ± 4.77[a]	30.17 ± 3.33[b] **	35.71 ± 3.59[a]	34.01 ± 4.17[a]	38. 71 ± 4.22[a]
RBCs ($\times 10^6/\mu l$)	5.11 ± 0.99[a]	2.29 ± 0.82[b c*]	4.51 ± 1.01[a]	4.31 ± 1.03[a]	4.61 ± 1.31[a]

*Values are expressed as mean ± S.D. n = 8 rats/group.
**Values not sharing a common superscript differ significantly at $p < 0.05$ (DMRT).
RRO: Ribes Rubrum Oil, Hb: hemoglobin, PCV: Packed cell Volume, RBCs: Red Blood Cells.

Table 6
Gastric tissues cyclooxygenase activity, prostaglandin E_2 concentration and cytochrome P450 reductase activity of normal and IND administrated groups.

Groups	Normal Control	Intoxicated Control	Treated with RRO		
Variables			5 ml/kg	10 ml/kg	15 ml/kg
Cox-2 ng/mg	4.56 ± 0.91[a]	2.01 ± 0.51[c**]	3.81 ± 0.33[b]	3.99 ± 0.41[b]	4.44 ± 0.28[a]
PGE_2 pg/mg	375.34 ± 55.14[a]	147.77 ± 10.14[c***]	371.13 ± 30.11[ab]	374.71 ± 31.61[a]	379.31 ± 39.11[a]
Cyto P450 ng/mg	9.45 ± 1.98[b]	19.23 ± 3.11[a**]	10.32 ± 1.42[b]	10.21 ± 1.73[b]	9.88 ± 1.66[b]

*Values are expressed as mean ± S.D. n = 8 rats/group.
**Values not sharing a common superscript differ significantly at $p < 0.05$ (DMRT).
RRO: Ribes Rubrum Oil, Cox: cyclooxygenase, PG: prostaglandin, Cyto: cytochrome.

linked with inhibitions in the synthesis of mucus, bicarbonate and phospholipids (Bilska-Wilkosz et al., 2013). These findings are in parallel with the findings from Inas et al. that exposure to acid accumulation of unprotected lumen in the stomach may help ulceration (Inas et al., 2011).

The production of free radicals is reported to have a crucial role in NSAID pathogenesis (Taye and Saad, 2009). In the current work, hematological values (Hb, PCV and RBCs) results were significantly ($p < 0.05$) reduced in indomethacin administrated rats compared to normal control. On the other hand, the ribes rubrum oil at doses (5, 10 and 15 ml) treated groups showed no significant difference of Hb, PCV and RBCs levels in comparison to normal control (Table 5). These results agreed with the findings of previous studies who reported that in the development of many illnesses reactive oxygen species production (ROS) plays an important role (Chakraborty et al., 2012; Uduak et al., 2012). Free radicals also cause damage to cellular antioxidant enzymes, which operate as the first line of cellular defense. During gastric ulceration this can lead to increased tissue damage (AlRashdi et al., 2012). Table 6 results are consistent with the results of previous study (Whittle, 2003). The defense and repair processes of the mucosa include the COX-2-induced ulcerated gastric mucosa, and that inhibition of the mucosa is delayed through a specific COX-2 inhibitor. COX-2 is only found in stomach mesenchymal cells such fibroblasts and ulcer border inflammatory cells, implying that COX-2 is an important part of the ulcer repair process expressed in mesenchymal cells along the ulcer's edge (Miura et al., 2004). Treatment with oil of ribes rubrum significantly inversed all subjects when comparing with indomethacin treated rats. These findings are in harmony with those obtained by prior results (Borrelli and Izzo, 2000). It revealed that flavonoids protege gastric mucosa injury by increase of prostaglandin mucosa levels and through inhibition by histidine decarboxylase of histamine release from mast cells. Ribes rubrum seems to have anti-inflammatory properties through decreasing the activity of COX-2 (Aneta et al., 2013). Ribes rubrum oil, substance, rich in phenolics, knowing to possess antioxidant activities (Gođevac et al., 2012; Leskinen et al., 2009). From Tables 1 and 2), data in this investigation demonstrated that ribes oil contain major phytoconstituents with high antioxidant activity, that responsible for the gastoprotective effect against indomethacin in rats.

The ribes rubrum oil administration in indomethacin rats offers a significant improvement on all parameters tested. In treated groups of rats, oils of 5 ml, 10 ml and 15 ml of the rubber were similar to normal levels of the levels of all parameters. The antioxidant characteristics of ribs rubrum oil can be ascribed to these outcomes, which rectify and remedy damaging rats' gastricity.

5. Conclusion

Gastric ulcers have become a complex condition and a serious socio-economic burden and face a huge difficulty in their treatment. A number of barriers have been encountered, including low effectiveness, numerous side effects and costs for gastric ulcers, with drugs and drugs for the treatment of gastric ulcer. Medical plants that are more secure, cost-effective and with low adverse effects are a replacement for gastric ulcers. Ribes rubrum oil therefore has a significant potential in combination with or alone, as a gastro-protective medication. It protected against the mucosal damage caused by indomethcin via its antioxidant characteristics and the ability to retain tissue and cellular integrity.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Adams, R., 2001. Identification of essential oils by gas chromatography quadrupole mass spectrometry. JASMS 16, 1902–1903.
AlRashdi, A.S., Salama, S.M., Alkiyumi, S.S., Abdulla, M.A., Hadi, A.H.A., Abdelwahab, S.I., et al., 2012. (2012) Mechanisms of gastroprotective effects of ethanolic leaf extract of Jasminum sambac against HCl/ethanol-induced gastric mucosal injury in rats. Evidence-Based Complem. Alternative Med.

Aneta, W., Jan, O., Magdalena, M., Joanna, W., 2013. Phenolic profile, antioxidant and antiproliferative activity of black and red currants (Ribes spp.) from organic and conventional cultivation. Int. J. Food Sci. Technol. 48 (4), 715–726.
Beutler, B., Greenwald, D., Hulmes, J.D., Chang, M., Pan, Y.-C.- E., Mathison, J., Ulevitch, R., Cerami, A., 1985. Identity of tumour necrosis factor and the macrophage-secreted factor cachectin. Nature 316 (6028), 552–554.
Bhattacharya, S., Chaudhuri, S.R., Chattopadhyay, S., Bandyopadhyay, S.K., 2007. Healing properties of some Indian medicinal plants against indomethacin-induced gastric ulceration of rats. J. Clin. Biochem. Nutr. 41 (2), 106–114.
Bilska-Wilkosz, A., Ochenduszka, M., Iciek, M., Sokołowska-Jeżewicz, M., Wiliński, B., Góralska, M., Srebro, Z., Włodek, L., 2013. Effects of acetylsalicylic acid on the levels of sulfane sulfur and non-protein sulfhydryl groups in mouse tissues. Pharmacol. Rep. 65 (1), 173–178.
Borrelli, F., Izzo, A.A., 2000. The plant kingdom as a source of anti-ulcer remedies. Phytotherapy Res.: Int. J. Devoted to Pharmacol. Toxicol. Eval. Natural Product Deriv. 14 (8), 581–591.
Chakraborty, S., Stalin, S., Das, N., Thakur Choudhury, S., Ghosh, S., Swarnakar, S., 2012. The use of nano-quercetin to arrest mitochondrial damage and MMP-9 upregulation during prevention of gastric inflammation induced by ethanol in rat. Biomaterials 33 (10), 2991–3001.
Chapman, D.G., Castillo, R., Campbell, J.A., 1959. Evaluation of protein in foods: 1. A method for the determination of protein efficiency ratios. Can. J. Biochem. Physiol. 37 (5), 679–686.
Chiang, L.-C., Ng, L.-T., Cheng, P.-W., Chiang, W., Lin, C.-C., 2005. Antiviral activities of extracts and selected pure constituents of Ocimum basilicum. Clin. Exp. Pharmacol. Physiol. 32 (10), 811–816.
Council, N.R., 1995. Prudent practices in the laboratory: Handling and disposal of chemicals. National Academies Press.
Cynthia, C., Ruth, L., Barbra, J., 1993. Laboratory tests and diagnostic procedures. WR Saunders Company.
De La Lastra, C.A., Barranco, M., Martin, M., Herrerias, J., Motilva, V., 2002. Extra-virgin olive oil-enriched diets reduce indomethacin-induced gastric oxidative damage in rats. Dig. Dis. Sci. 47, 2783–2790.
Drabkin, D.L., 1949. The standardization of hemoglobin measurement. Am. J. Med. Sci. 292, 386–399.
El-Metwally, E.M., 2014. Evaluation of antiulcer activity of ginger, clove and castor oils against aspirin induced gastric ulcers in rats. World Appl. Sci. J. 29, 815–824.
Fan, Y.-Y., Chapkin, R.S., 1998. Importance of dietary γ-linolenic acid in human health and nutrition. J. Nutr. 128, 1411–1414.
Gođevac, D., Tešević, V., Vajs, V., Milosavljević, S., Zdunić, G., ĐOrđević, B., et al., 2012. Chemical composition of currant seed extracts and their protective effect on human lymphocytes DNA. J. Food Sci. 77, C779–C783.
Goffman, F.D., Galletti, S., 2001. Gamma-linolenic acid and tocopherol contents in the seed oil of 47 accessions from several Ribes species. J. Agric. Food. Chem. 49 (1), 349–354.
Grassi, J., Roberge, C.J., Frobert, Y., Pradelles, P., Poubelle, P.E., 1991. Determination of ILlα, ILlβ and IL2 in biological media using specific enzyme immunometric assays. Immunol. Rev. 119, 125–145.
Green, L.C., Wagner, D.A., Glogowski, J., Skipper, P.L., Wishnok, J.S., Tannenbaum, S. R., 1982. Analysis of nitrate, nitrite, and [15N] nitrate in biological fluids. Anal. Biochem. 126 (1), 131–138.
Haithem, A., Farghali, H., Shimaa, F., Ghozy, E., El-Mehiry, H., 2014. Study the effect of basil oil as herbal treatment of acetylsalicylate induced gastric ulcer in experimental rat. Model Global Vet 12, 431–448.
Hamberg, M., Samuelsson, B., 1973. Detection and isolation of an endoperoxide intermediate in prostaglandin biosynthesis. Proc. Natl. Acad. Sci. 70 (3), 899–903.
Helmy, H., 2011. Study the effect of fenugreek seeds on gastric ulcer in experimental rats. World J. Dairy Food Sci. 6, 152–158.
Hemler, M., Lands, W.E., 1976. Purification of the cyclooxygenase that forms prostaglandins. Demonstration of two forms of iron in the holoenzyme. J. Biol. Chem. 251 (18), 5575–5579.
Inas, Z., Hala, A., Gehan, H.H., 2011. Gastroprotective effect of Cordia myxa L. fruit extract against indomethacin-induced gastric ulceration in rats. Life Sci. J. 8, 433–445.
Khan, I.A., Jahan, P., Hasan, Q., Rao, P., 2019. Genetic confirmation of T2DM meta-analysis variants studied in gestational diabetes mellitus in an Indian population. Diabetes Metab. Syndr. 13 (1), 688–694. https://doi.org/10.1016/j.dsx.2018.11.035.
Kiliç, F.S., Sirmagül, B., Batu, Ö., Erol, K., 2006. Dose-dependent effects of verapamil on ethanol-induced gastric lesions in rats. J. Health Sci. 52 (6), 781–786.
Leskinen, H.M., Suomela, J.-P., Kallio, H.P., 2009. Effect of latitude and weather conditions on the regioisomer compositions of α-and γ-linolenoyldilinoleoylglycerol in currant seed oils. J. Agric. Food. Chem. 57 (9), 3920–3926.
Makarova, N.V., Eremeeva, N.B., 2015. Antioxidant activity and chemical composition of black currant and raspberry of Samara's Region, 2014. Am.-Eurasian J. Sustain. Agric., 22–28
Makri, O., Kintzios, S., 2008. Ocimum sp. (basil): Botany, cultivation, pharmaceutical properties, and biotechnology. J. Herbs Spices Med Plants 13 (3), 123–150.
Malenčić, D., Popović, M., Miladinović, J., 2007. Phenolic content and antioxidant properties of soybean (Glycine max (L.) Merr.) seeds. Molecules 12 (3), 576–581.
Mc-Inory, M., 1954. A micro hematocrit for determination the packed cell and hemoglobin concentration on capillary blood. J. Clin. Biochem. 32.
McLean, A.M., Day, P.A., 1974. The use of new methods to measure: the effect of diet and inducers of microsomal enzyme synthesis on cytochrome P-450 in liver homogenates, and on metabolism of dimethyl nitrosamine. Biochem. Pharmacol. 23 (7), 1173–1180.
Miura, S., Tatsuguchi, A., Wada, K., Takeyama, H., Shinji, Y., Hiratsuka, T., Futagami, S., Miyake, K., Gudis, K., Mizokami, Y., Matsuoka, T., Sakamoto, C., 2004. Cyclooxygenase-2-regulated vascular endothelial growth factor release in gastric fibroblasts. American Journal of Physiology-Gastrointestinal and Liver. Physiology 287 (2), G444–G451.
Nour, V., Trandafir, I., Ionica, M.E., 2011. Ascorbic acid, anthocyanins, organic acids and mineral content of some black and red currant cultivars. Fruits 66 (5), 353–362.
Okewumi, T.A., Oyeyemi, A.W., 2012. Gastro-protective activity of aqueous Carica papaya seed extract on ethanol induced gastric ulcer in male rats. Afr. J. Biotechnol. 11, 8612–8615.
Paccalin, J., Dabadie, H., Bernard, M., Mendy, F., Spielmann, D., Delhaye, N., 1985. Intérêt d'une nouvelle plante oleagineuse: l'onagre. Apport en acide gamma-linolenique et troubles de la désaturation en pathologie. Med. Nutr. 21, 132–136.
Parmar, N., Desai, J.K., 1993. A review of the current methodology for the evaluation of gastric and duodenal anti-ulcer agents. Indian J. Pharmacol. 25, 120.
Snedecor, G., Cochran, W., 1969. Statistical methods. The Iowa State University Press, Ames Iowa USA.
Solomon, L.Z., Jennings, A.M., Hayes, M.C., Bass, P.S., Birch, B.R., Cooper, A.J., 1998. Is gamma-linolenic acid an effective intravesical agent for superficial bladder cancer? In vitro cytotoxicity and in vivo tolerance studies. Urol. Res. 26 (1), 11–15.
Takada, R., Saitoh, M., Mori, T., 1994. Dietary γ-linolenic acid-enriched oil reduces body fat content and induces liver enzyme activities relating to fatty acid β-oxidation in rats. J. Nutr. 124, 469–474.
Takeuchi, K., Ueshima, K., Hironaka, Y., Fujioka, Y., Matsumoto, J., Okabe, S., 1991. Oxygen free radicals and lipid peroxidation in the pathogenesis of gastric mucosal lesions induced by indomethacin in rats. Digestion 49 (3), 175–184.
Taye, A., Saad, A.H., 2009. Role of rosiglitazone as a gastroprotective agent against indomethacin-induced gastric mucosal injury in rats. Gastroenterology Res. 2, 324.
Uduak, E.U., Timbuak, J., Musa, S., Ikyembe, D., Abdurrashid, S., Hamman, W., 2012. Ulceroprotective effect of methanol extract of Psidium guajava leaves on ethanol induced gastric ulcer in adult wistar rats. Asian J. Med. Sci. 4, 75–78.
Velioglu, Y.S., Mazza, G., Gao, L., Oomah, B.D., 1998. Antioxidant activity and total phenolics in selected fruits, vegetables, and grain products. J. Agric. Food. Chem. 46 (10), 4113–4117.
Wang, Z., Hasegawa, J., Wang, X., Matsuda, A., Tokuda, T., Miura, N., et al., 2011. Protective effects of ginger against aspirin-induced gastric ulcers in rats. Yonago acta medica 54, 11.
Whittle, B.J., 2003. Gastrointestinal effects of nonsteroidal anti-inflammatory drugs. Fundam. Clin. Pharmacol. 17, 301–313.