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Gastroprotective Activity of $NiCr_2O_4$

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Abstract

In today's world, peptic ulcer is seen as a widespread issue. The rise in peptic ulcer cases is a direct outcome of how modern, civilised lifestyles influence people to have more stressful and less active lives [1]. Between three and ten percent of people may develop stomach ulcers. There are 15,000 annual fatalities worldwide due to peptic ulcers [2]. There are over 3.6 lakh new ulcers cases reported annually, and about four million individuals admitted to hospitals in the US each year due to PUD [3]. In male to female ratio of 3:1, duodenal ulcers are more common in men, but stomach ulcers are more common in women (1.5:2.1) [4].

Keywords: Gastroprotective agents • $NiCr_2O_4$ • Gastroprotective activity • Peptic ulcer

Introduction

When the gastrointestinal tract (GIT) is out of whack with protective and harmful (aggressive) elements, peptic ulcers form. Aggressive factors outweigh protective ones in the gastrointestinal tract, leading to PUD [5].

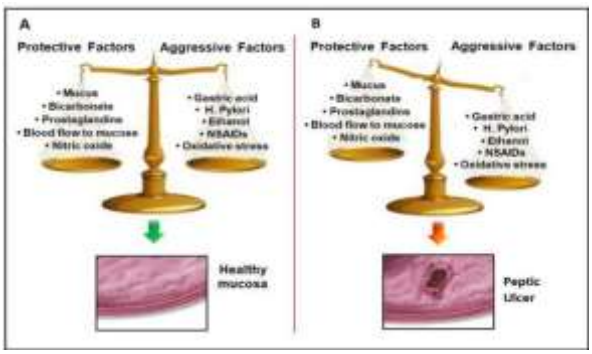

Figure 1. Factors involved in the pathological process of peptic ulcer.

Gastric mucosal protection

The gastromucosal layer plays a pivotal role in ulcer prevention. Consequently, the acid does not reach the layers of the stomach. Because of their close proximity to one another, epithelial cells and cells that line the mu limit the acid attack on the stomach [6]. To aid in the healing process, prostaglandins stimulate the production of bicarbonate, enhance blood flow to the injured mucosal cells, and stimulate the release of gastric mucus. This proves that prostaglandins have a cytoprotective effect [7,8,9,10].

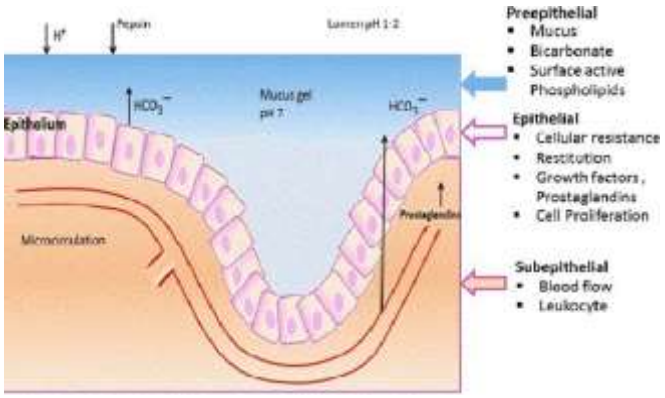

Figure 2. Factors associated with gastro mucosal defense and repair free radicals and their role in causing peptic ulcer.

Acute stomach ulcers caused by ethanol, experimental stress, or NSAIDS are thought to have ROS as a major pathogenic factor. Gastritis severity in helicobacter pylori infections is inversely proportional to ROS liberation excess [11]. These oxygen radicals inhibit the GIT's protective stomach mucosal capability, which helps to avoid ulcers. Transferring iron or copper ions to albumin, plasmin, or ferritin increases oxidative damage by creating radicals that are free like OH [12]. Here is the process by which these free radicals create ulcers.

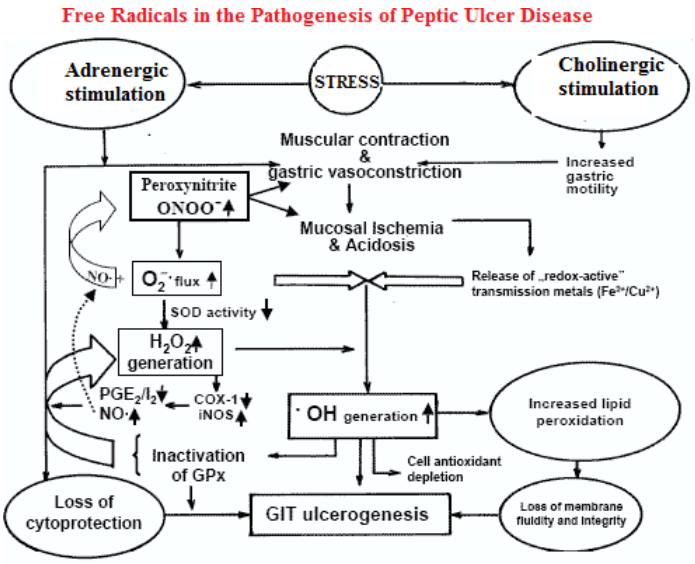

Figure 3. Free radicals in the pathogenesis of Peptic Ulcer

Although some theories have been put up on occasion, the exact biochemical changes that occur during the development of ulcers remain unclear. Ulcer formation may be influenced by stress-induced changes in stomach motility, mast cell degranulation, and prostaglandin levels [13]. Experimental stomach injury caused by ischaemia and reperforation, hemorrhagic shock, and ethanol administration has also shown the involvement of oxygen-derived free radicals [14].

The mucosal damage induced by NSAIDs was unrelated to the acid as small intestines do not have any cells that secrete acid. Nonsteroidal anti-inflammatory medications, or NSAIDs, cause mucosal damage in the small intestine, so it is recommended to consider alternative pharmaceuticals in addition to protons pump inhibitors and histamines 2 receptor inhibitors, which are traditional acid-reducing treatments (PPIs) [18].

The ulcer treatment regimen typically consists of H2RAs and proton pump inhibitors. Unfortunately, they sometimes come with unpleasant side effects such as a rash, discomfort, and diarrhoea. Further, H2RAs have been linked to negative effects on the genitourinary, cardiovascular, central nervous system, and other important organ systems [19]. Their use with proton pump inhibitors (PPIs) increases the danger of "acid rebound phenomenon" when therapy ends, in addition to the negative central nervous system, ear, nose, and gastrointestinal tract (GI) [20]. Mucosal protective medications, such nevertheless, they all have their own set of limitations and side effects, in addition to antisecretory therapies as H2RAs, antimuscarinic agents, proton pump inhibitors. Reconciliation of epithelial layers and underlying connective tissues is necessary for the healing of peptic ulcers. This process involves proliferation of cells, migration, and differentiation [21].

The current gold standard for ulcer therapy, which mostly includes H2RAs and PPA, does not allow for this. The present study mainly focusses on antioxidant therapy alone, not in combination with other therapies. Recently, herbal medicines have been featured prominently in the media. Therapeutic treatment extracts are consistently less toxic than synthetic pharmaceuticals, according to animal research. This is the main advantage of herbal remedies. The purpose of developing ulcer models based on characteristics associated with ulcer aetiology is to investigate the potential anti-ulcer effects of newly identified medications and chemicals. Stress, alcohol, nonsteroidal anti-inflammatory drugs (NSAIDs) endogenous glutathione (GSH), and catalase are some of the enzymes that work together to lower ROS levels, which are harmful to tissues. The most common disorder affecting the upper gastrointestinal tract is peptic ulcer disease, which has a high incidence rate globally. As far as health is concerned, it has been rather serious.

Throughout their lifetimes, 8–11% of women and 11–14% of men will have peptic ulcers. In the United States, 4% to 10% of the population has gastric ulcers, whereas 3% to 5% of those with peptic ulcers have duodenal ulcers. Although most stomach ulcers start between 45 and 55 years old, duodenal ulcers usually appear in individuals between 20 and 50 years old. Four in ten Americans have heartburn monthly, and fourteen percent use medication for indigestion at least twice a week. The incidence of hospitalisation in the US caused by peptic ulcer has dropped from 25.2 per 10,000 to 14.2 per 10,000. With the advent of many antiulcer medications and more precise diagnostic methods, the peptic ulcer mortality rate has dropped from 3.5 per 100,000 to 1.1 per 100,000 . The development of stomach ulcers may be influenced by mucosal ischaemia. The fact that prostaglandins enhance blood flow, bicarbonate production, and mucus secretion—three factors that aid in the repair and regeneration of mucosal cells—is well recognised. Consequently, gastritis and stomach ulcers may occur when there is a lack of these nutrients, which can be caused by NSAIDs or other irritants.

On the other side, there can be other reasons for reduced bicarbonate or mucus output. Some subsets of stomach ulcer sufferers have these issues. Modern medicine is making great use of novel medicinal formulations that function at the nanoscale. There is a vast array of distinctive physical, chemical, and biological properties shown by nanoparticles (NPs). Among the most promising nanomaterials are AgNPs due to their anti-inflammatory, antifungal, and antiviral characteristics, in addition to their efficient antibacterial activity against several microorganisms. Pemphigus, toxic epidermal necrolysis, chronic ulcers, and burns are just some of the skin disorders that NPs have shown promise in treating, according to a number of studies. Therefore, this work set out to use a variety of in vivo methodologies to assess the biological impacts of mineral nanoparticles like NiCr2o4 and CaCr2o4 NPs

Methodology

Experimental animals

Male or female albino Wistar rats assessing (150-200) g.m were sourced from Sainath Agency, Musheerabad, and used in the present work. The rats were provided with water at all times .The rats were starved for 48 hours after being habituated to the facility for a week. Without approval from the appropriate institutional ethics committee, the research could not go forward ((1567/PO/Re/S/11/CPCSEA)). Although they were fasted for 24 hours before to the trial, the animals were accepted unlimited access to water. The experimental room at the animal facilitation facility at the Marri Laxman Reddy Institute of Pharmacy in Dundigal, Hyderabad, was the site of the study.

Drugs

A gift sample of ranitidine was obtained from Dr. Reddy's laboratory in Hyderabad. In this antiulcer evaluation, Ca2Mno4 and CaMn204 nanoparticles were used.

Chemicals

- Conical flasks (Titration flask)
- Micro burettes
- Volume measuring glass tubes
- 10ml, 50ml beakers
- Glass cylinders
- Centrifuge tubes
- Droppers
- Wattman filter paper
- Desiccators for anesthesia
- Distilled water
- Weighing Machine

The analytical grade chemicals and reagents were sourced from authorized agents/suppliers.

Pylorus-ligation induced Ulcer model

Rats were divided into five groups (n=6 in each group).

- Rats were divided into five groups (n=6 in each group).
- Group I: Negative control (normal saline 1 ml)
- Group II: Positive control (normal saline 1 ml)
- Group III: Pylorus ligation + Ranitidine (30 mg/kg, orally)
- Group IV: Pylorus ligation + $NiCr_2O_4$ NP's (200 mg/kg, orally) Group V: Pylorus ligation + CaCr2O4 NP's (200 mg/kg, orally)

Gastric volume and pH

The amount of liquid inside the supernatant was quantified. Using a pH meter with a 2.0-4.5 and 5.0-8.5 range, with a 0.5 difference, the stomach fluids' pH levels were determined.

Total and free acidity

Using phenolphthalein and Toffer's reagent as indicators, 5 ml of diluted gastric juice was titrated with 0.01N NaOH using a micro burette. The goal was to determine the total and free acidity until a persistent pink colour was detected for the former and a canary yellow colour for the latter. The clinical units of acidity were defined as the quantity of 0.01N NaOH base needed to titrate 100 mL of stomach output.

$$\text{Total acidity} = \frac{\text{volume of NaOH}^{*}}{0.1}\ \text{Normality}\ {}^{*}100\ \text{mEq/L}$$

Ulcer score

The incidence and grading of ulcers was done according to the method described by Wilhelmi and Menasse-Gadyni (1972). Necro-hemorrhagic spots greater than 2 mm diameter was taken as ulcer. These are graded as follows:

- 0.5-Minute, sporadic, punctuate lesions
- 1 - Several small lesions
- 2- One large extensive lesion, or multiple moderate sized lesions
- 3- Several large lesions.

Ulcer indexes

Ulcer index was determined by method of Ganguly and Bhatnagar

$$\text{Ulcer index} = \frac{10}{X}$$

$$\text{where, } X = \frac{\text{total mucosal area}}{\text{total ulcerated area}}$$

Gastric wall mucous content:

A significantly modified version of the way outlined by Corne et al. was used to quantify the quantity of stomach wall mucus. After immersing for two hours in a solution containing the stomach is opened along its greater curvature, and then weighed and immersed. The extra color was then rinsed off using two 0.25 M sucrose solutions, one at 15 minutes and the other at 45 minutes intervals. 0.5M $MgCl_2$ was used to remove any remaining dye complexed with the stomach

mucous after 2 hours of shaking every 30 minutes. A spectrometer after equal volumes of diethyl ether and shaking of the blue extract. A standard curve was used to compare the absorbance of each solution, which allowed us to calculate the various dye concentrations and weights (in milligrams). It was then determined by dividing the weight of the dye by the weight of the stomach.

Results

Nanoparticles of NiCr2O4 and Their Impact on Rats with PL-Induced Ulcers

At dosages of 200 mg/kg, NiCr2O4 nanoparticles were tested for their antiulcer efficacy in a rat model of pylorus ligation-induced ulcers.

Impact on ulcer table

By significantly raising the percentage of ulcer protection to 76.0±1.12, CaCr204 200 mg/kg significantly reduced the ulcer index. The T.No.1 shows the outcomes.

Impact on Gastric quantity

The amount of gastric juice was reduced by NiCr2O4 200 mg/kg although the difference was striking when compared to the control. A significant decrease in stomach content volume has been seen with ranitidine at a dosage of 10 mg/kg. The results are shown in table 2.

Impact on pH of gastric liquid

At a dosage of 200 mg/kg, CaCr204 significantly raised the pH of the gastric juice to 2.85 ± 0.43. The findings may be seen in the Table 2.

Impact on available acidity & total tartness

At a dose of 600 mg/kg, CaCr204 significantly decreased acidity (free and total) ($p<0.01$), which was comparable to the effect of the conventional medicine ranitidine (10 mg/kg) on rats ($p<0.01$). The outcomes may be shown in table 2.

Table 1. Effect of $CaCr_2O_4$ Nanoparticles on Pylorus ligation ulcer model in rats

Treatment	Dose (mg/kg)	Ulcer index	% ulcer inhibition
Control	10 m/kg	1.25 ± 0.15	-
$NiCr_2O_4$NP′s	200	0.74 ± 0.48	$40.8 \pm 0.73^{**}$
Ranitidine	10	0.00	$100 \pm 0.42^{***}$

Results are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Tukey- kramer multiple comparison test.

Table 2: Effect of $CaCr_2O_4$ Nanoparticles on Antisecretory parameters

Treatment	Dose (mg/kg)	Gastric volume (m/100 g)	**pH**	Free acidity (mEg/L/**l00**)	Total acidity (mEg/L/**l00**)
Control	10ml/kg	2.64 ± 0.11	1.45 ± 0.31	61.26 ± 4.3	80.76 ± 3.5
$NiCr_2O_4$ NP's	200	$2.81 \pm 0.16^{*}$	$1.49 \pm 0.74^{**}$	59.91 ± 3.8	77.35 ± 3.16
Ranitidine	10	$1.61 \pm 0.06^{**}$	$4.31 \pm 1.62^{**}$	$21.64 \pm 3.6^{**}$	$32.18 \pm 3.1^{**}$

Results are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Tukey-kramer multiple comparison test.

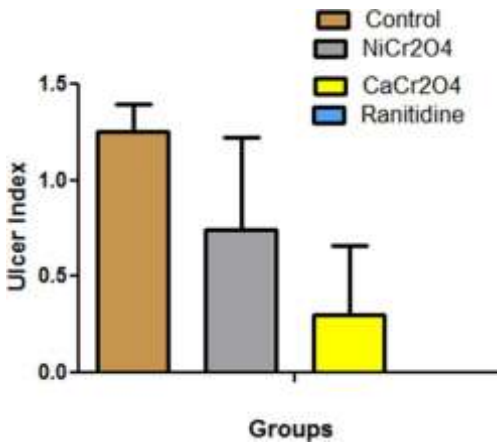

Figure 4. Effect of NiCr2O4 Nanoparticles on ulcer index in pylorus ligation induced ulcer model in rats.

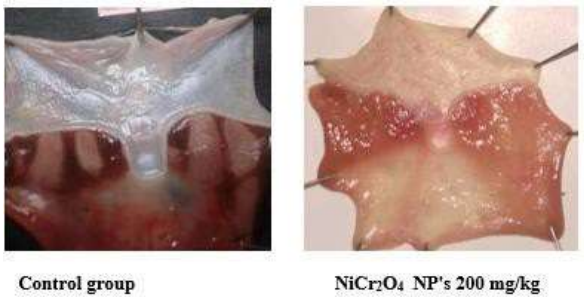

Figure 3. Morphological appearance of gastric ulcers in pylorus ligation induced stomach ulcers in rats

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