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Anti-Ulcer Activity of Pantoprazole in Ethanol-Induced Ulcer Model

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Abstract: *This study tried to look at the non-acid-dependent gastroprotective, antioxidant, and anti-inflammatory effects of pantoprazole, in an absolute ethanol–induced acute gastric ulcer model using Wistar rats. In the beginning, fasted rats were split into five groups: normal control, ulcer control, low-dose pantoprazole (20 mg/kg) , high-dose pantoprazole (40 mg/kg) , and an omeprazole reference group (20 mg/kg). The pre-treatments were given by mouth , about one hour before the animals received the chemical injury , which was done using absolute ethanol.*

When the results came in, the high-dose pantoprazole group showed almost striking gastroprotective activity, with fewer gross mucosal bleeding streaks and it reached an 82.76% Percentage Gastroprotection. On the biochemical side, pantoprazole pre-treatment markedly reduced malondialdehyde build-up, and it also helped keep the natural antioxidant defense system working—this was seen through preserved reduced glutathione, plus better maintenance of superoxide dismutase, catalase, and carbonic anhydrase actions. Beyond that, the immunoassay outcomes suggested a clear reduction in inflammatory mediators, including TNF-α, IL-1β, IL-6, and when histopathology was reviewed, tight junction structure was kept in place while neutrophil entry was noticeably lowered. Overall, the findings suggest that pantoprazole offers strong, dose-related cell protection against direct chemical necrosis, mainly through body-wide antioxidant and anti-inflammatory pathways, and not by relying on gastric acid suppression at all.

Keywords: Pantoprazole, Gastroprotection, Ethanol-induced gastric ulcer, Oxidative stress, Pro-inflammatory cytokines, Cytoprotection.

I. INTRODUCTION

The stability and functional capacity of the gastric mucosa is tied to a steady homeostatic sort of balance between mean luminal factors and internal defensive systems. The stomach basically has to keep the luminal gastric juice at an exceptionally low pH, usually somewhere between 1.5 and 2.0, to help start proteolysis and also get rid of the ingested microbial pathogens. But to actually endure that kind of hostile setup, the gastric wall leans on a multi-tiered defensive framework, kind of arranged into pre-epithelial , epithelial, and post epithelial protective zones. The pre-epithelial portion is made from a thick continuous mucus gel layer, and inside it is secreted bicarbonate ions, (HCO_3^-), which build a physical buffer zone. This buffer helps keep a near-neutral pH gradient right next to the tissue surface, so the tissue doesn't get hit too hard. The epithelial line depends on a tight monolayer of columnar cells stuck together by paracellular junction structures; these are physical tight junctions. Within those tight junctions there are transmembrane claudins, and occludins as well, plus the whole thing is backed by high mitotic regeneration rates, so the layer can repair itself fast. Underneath all that, the post-epithelial defense stage uses a dense microvascular capillary network. That network brings oxygen, clears away noxious metabolic byproducts, and triggers rapid vasodilatory Hyperemia to basically wash out back diffused protons before they get the chance to cause deeper tissue injuries.

When aggressive forces overpower these localized protective systems , the whole balance just kind of breaks down and then it starts the pathological cascade behind Peptic Ulcer Disease (PUD). In clinic terms, PUD shows up as a big worldwide health problem, often with severe epigastric pain , nausea and sometimes even deadly complications, like

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gastrointestinal perforation, or severe bleeding from inside the lumen. For the long-lasting chronic form, the drivers are usually *Helicobacter pylori* infection, or the overuse of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). But acute, erosive gastritis, plus those severe mucosal lesions, tend to happen after sudden ingestion of concentrated necrotizing substances, alcohol misuse, or severe physiological stress, kind of all at once. In day-to-day management of acid related mucosal issues, proton pump inhibitors (PPIs) are relied on heavily, especially pantoprazole. Pantoprazole is basically an inactive lipophilic prodrug it just builds up selectively inside the highly acidic secretory canaliculi of parietal cells. After it gets protonated and then activated into a reactive sulfenamide , it makes covalent disulfide bonds with chosen cysteine residues on the H^+/K^+-ATPase pump. That shuts down the last acid secretion step, permanently, so tissue repair can proceed through passive healing.

While the clinical usefulness of pantoprazole is solidly established for acid-driven disorders, figuring out how far its cytoprotective effects go needs models that actually check what it does when acid is not the main problem. An absolute ethanol–induced gastric ulcer assay is often used as a sort of benchmark for this, because it skips the usual acid hypersecretory routes and instead makes lesions through direct chemical necrosis. When strong alcohol spills into the gastric lumen, its amphiphilic behavior lets it quickly "unmake" the mucus shield that sits in front of the epithelium, and it also solubilizes the lipid bilayers on the surface epithelial cells. So, you get an immediate, almost structural collapse. But it is not only straightforward cytotoxicity. Ethanol can also push deeper into the lamina propria where it injures microvascular endothelial cells. That harm then sets off fast platelet activation , followed by capillary blockage and the appearance of microthrombi, so local perfusion drops, leading to tissue ischemia. And once ischemia is present, the remaining cells lose oxygen, which blocks metabolic recuperation and makes necrotic progression speed up.

Oxidative stress and lipid peroxidation act like the main chemical triggers for tissue destruction in the ethanol model, basically. Inside the sub cellular metabolism, alcohol processing can generate an overabundance of reactive oxygen species, also ROS, such as superoxide anions and very reactive hydroxyl radicals. These loose free radicals then go after the polyunsaturated fatty acids, the PUFAs, found in both cellular and mitochondrial membranes. After that they start a kind of self-amplifying chain reaction that turns normal structural lipids into harmful aldehydes, especially Malondialdehyde, or MDA. As the membrane lipids get altered, the mitochondrial proton motive gradient is disrupted. Because of that, ATP synthesis drops sharply , and the cell ends up with an energy shortfall. That failure then supports the opening of transition pores, so Cytochrome c can escape into the cytosol, which kicks off caspase cascades and results in programmed cell death. At the same time, the rapid ROS burst quickly uses up the tissue's own antioxidant defenses, which means reduced glutathione, the GSH pools, get drained. It also ends up inactivating protective enzymes like Superoxide Dismutase, aka SOD, and Catalase.

This cellular harm and oxidative collapse set off a rather intense inflammatory reaction across the mucosal layer. When ischemic, damaged cells appear, they activate the transcription factor Nuclear Factor kappa B (NF-κB) and it then moves into the cell nucleus. There it ramps up, basically increases, the production of several pro-inflammatory cytokines , like Tumor Necrosis Factor-alpha (TNF-α), Interleukin-1 beta (IL-1β), and Interleukin-6 (IL-6). These mediators boost the expression of cell adhesion molecules on the vascular endothelium, so circulating neutrophils start to roll, then stick, and finally push through—migrating out of the capillaries and into the lamina propria. After they're inside the tissue, the stimulated neutrophils release Myeloperoxidase (MPO) and hypochlorous acid, and that stuff can degrade the extracellular matrix. As a result, the necrotic zone gets larger, and shallow erosions end up turning into deeper, actively bleeding ulcers.

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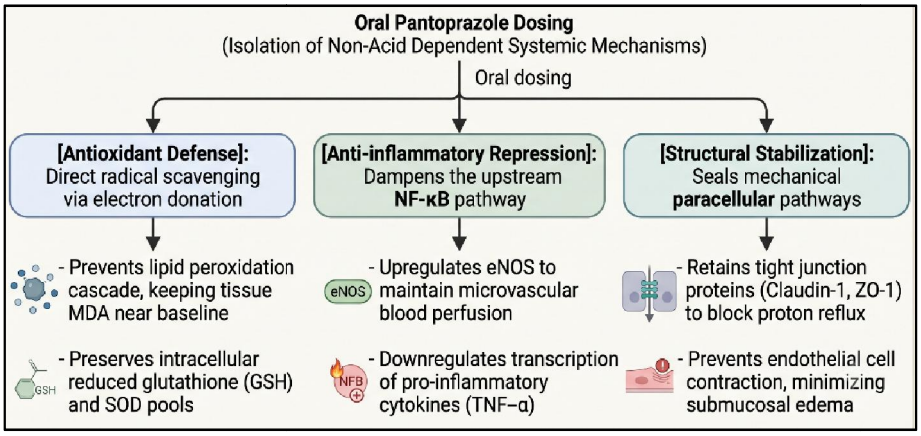

Figure. 1 Pantoprazole Multi-Tiered Gastroprotective Paradigm.

Some emerging, experimental evidence suggests that pantoprazole's therapeutic effect might go beyond just proton pump inhibition, it also seems to have really independent cytoprotective actions. The drug's chemical make-up, with an electron dense benzimidazole ring plus a sulfinyl bridge, may let it behave like a sort of direct electron donor, meaning it can scavenge reactive free radicals before these species go after membrane lipids. In practice, by reducing lipid peroxidation it can help keep mitochondrial integrity more stable, so cells keep the energy needed for fast repair of damaged areas, and it also helps block apoptotic sequences. At the same time, pantoprazole appears to lower the expression of endothelial adhesion molecules, which limits neutrophil attachment and reduces the tissue MPO build up.

Even though the acid-suppressing properties of pantoprazole have been well described, its ability to directly counteract chemical necrosis, keep the endogenous antioxidant reserves from dropping , and also fine-tune pro-inflammatory cytokine signaling still calls for a more complete and careful check. In other words, confirming these non-acid related cytoprotective routes gives the main clinical reason for using pantoprazole when dealing with acute chemical, or stress-triggered erosive gastritis. So, this exploratory work is set up to evaluate in a stepwise dose-dependent manner the anti-ulcer effect and general gastroprotective activity of pantoprazole in rodents, specifically against absolute ethanol induced gastric damage, while also mapping its structural traits, biochemical signatures and molecular patterns, in order to justify its broader translational potential.

II. DRUG PROFILE

Pantoprazole sodium ($C_{16}H_{14}F_2N_3NaO_4S$) is a sort of chemically tuned substituted benzimidazole derivative , that shows up in the pharmacological class of proton pump inhibitors (PPIs). In terms of layout, the molecule has a benzimidazole core , and it is tied through a methylsulfinyl bridge to a substituted pyridine ring. You also have particular chemical adjustments, meaning there is a difluoromethoxy placement on the benzimidazole part and dimethoxy groups sitting on the pyridine side. Because of those, the compound tends to stay more chemically stable at a neutral , or maybe a slightly acidic pH , than the earlier generation PPIs such as omeprazole. This extra stability reduces accidental early, non-specific activation when the environment is neutral. So, the result is a more precise, body targeted action.

Pharmacokinetically, pantoprazole is basically given as a kind of inactive, lipophilic prodrug thing. After oral ingestion and subsequent absorption in the small intestine, it ends up moving through the systemic bloodstream pretty unchanged, at a physiological pH around 7.4. In that neutral situation, the molecule is mostly non ionized and it doesn't show the kind of systemic toxicity you might worry about. Because it is lipophilic, it can diffuse across the basolateral membranes of the gastric parietal cells, and it then pools inside the very acidic secretory canaliculi where the pH falls under 2.0. In there, the pyridine and benzimidazole nitrogens get protonated quickly, so the ionized drug is kind of

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trapped within the canaliculus and the concentration can increase up to 1,000-fold. After that, the protonated structure rearranges, driven by acid catalysis, into a reactive positively charged tetracyclic sulfenamide intermediate.

This active sulfenamide intermediate acts like an irreversible enzyme blocker, sort of. It ends up making covalent disulfide bonds, the -S-S- type, with the sulfhydryl group(s) on certain cysteine residues, found on the extracellular loop of the gastric H^+/K^+-ATPase pump the proton pump. Pantoprazole mostly hooks onto Cysteine-813 which is the one that physically blocks the ion transport channel, and also onto Cysteine-822 which kind of locks the enzyme's conformational arrangement in place. So, by binding irreversibly to the terminal step of the acid secretion pathway, pantoprazole reduces both basal and evoked gastric hydrochloric acid release, regardless of what the main secretory trigger is, whether that is histamine, gastrin, or acetylcholine. Acid output can only restart after parietal cells build new H^+/K^+-ATPase complexes, giving that long pharmacodynamic tail that goes beyond the drug's brief systemic half-life of about one hour.

Beyond its main acid reducing effects, pantoprazole also shows independent, non-acid type cytoprotective activity, so it can work even when the injury is more direct chemical, sort of trauma. The electron dense benzimidazole ring along with the sulfinyl bridge helps the molecule behave like a direct electron donor. In that way it can mop up reactive oxygen species, for example superoxide anions, and also hydroxyl radicals. By doing that, the oxidative chain reaction like lipid peroxidation gets stopped, intracellular reduced glutathione (GSH) stores are kept steadier, and several important antioxidant enzymes stay stabilized, instead of being knocked out too easily.

On top of the scavenging effect, pantoprazole reduces the nuclear travel (translocation) of Nuclear Factor kappa B (NF-κB) which then lowers the transcription of multiple pro inflammatory cytokines (TNF-α, IL-1β, IL-6). At the same time, it suppresses endothelial adhesion molecules, such as (ICAM-1). When you put these pieces together, neutrophil infiltration becomes less likely and the tissue edema response is muted, so the stomach wall structures are better defended against intense chemical aggression.

III. MATERIALS & METHOD

Experimental Animals and Ethical Governance: Healthy adult Wistar albino rats, about 180-220 g, were used with equal sex distribution. They were kept in polypropylene cages, with autoclaved paddy husk bedding, under controlled parameters, like 24 ± 2°C temperature, 50-60 % humidity, and a 12-hour light dark cycle. The animals had free access to a standard pellet diet plus deionized water. Every procedure was approved by the Institutional Animal Ethics Committee (IAEC), under protocol reference number **IAEC/2026/P-45**, and it was done in line with CPCSEA guidelines.

Chemicals and Reagents: The pure reference standard, pantoprazole sodium ,and the reference standard omeprazole sodium, were got from Sigma-Aldrich. For the solvents and matrix, absolute ethanol (99.9% v/v) was purchased from Merck along with sodium carboxymethylcellulose, or CMC. The high-sensitivity biochemical assay kits for measuring tissue Malondialdehyde, MDA , Reduced Glutathione , GSH , Superoxide Dismutase, SOD , and Catalase, CAT , were obtained from Cayman Chemical. Rat specific solid phase sandwich ELISA kits for TNF-α, IL-1β, and IL-6 were sourced from R&D Systems.

Experimental Design and Treatment Dosing: Thirty rats were put into five parallel groups at random (n = 6 per group) with a kind of automated block-randomization program. Before dosing, all animals went through a strict 24-hour fasting routine in elevated wire mesh cages to help clear the gastric lumen and also reduce coprophagy, I mean you know, the usual idea. For dosing, suspensions were made fresh each day using a 0.5% w/v CMC vehicle and then given via an 18-gauge curved intragastric gavage needle. The administration volume stayed the same each time at 5 mL/kg of body weight:

- Group I (Normal Control): Vehicle only, no chemical mucosal trauma.
- Group II (Ulcer Control): Vehicle pre-treatment followed by absolute ethanol challenge.

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- Group III (Low-Dose Pantoprazole): Pantoprazole at 20 mg/kg body weight p.o.
- Group IV (High-Dose Pantoprazole): Pantoprazole at 40 mg/kg body weight p.o.
- Group V (Reference Control): Omeprazole at 20 mg/kg body weight p.o.

Acute Ulcer Induction and Tissue Processing: About 60 minutes following the oral dosing of the relevant pre-treatments, acute mucosal injury was brought on in Groups II, III, IV, and V through oral gavage delivering 1.0 mL of pure ethanol. Group I, meanwhile, got the same amount of distilled water . Roughly 60 minutes after the ethanol, the animals were humanely euthanized using an overdose of isoflurane. Then, midline laparotomies were carried out, stomachs were removed, split open along the greater curvature, gently flushed with ice-cold normal saline, and laid out flat on wax trays for assessment.

Macroscopic Gross Evaluation: Gross mucosal injury, shown as longish linear hemorrhagic streaks along with petechiae, was assessed under a stereomicroscope at (×10) by two separate independent pathologists , both blinded. They applied a semi-quantitative scoring ladder where 0: Normal and 4: Severe confluent necrosis. The resulting lesion scores were then used to estimate the visual Ulcer Index (UI) and to compute the exact Percentage Gastroprotection for each treated cohort compared to the untreated ulcer control group , essentially the baseline.

Tissue Biochemical and Immunoassay Profiling: The excised gastric samples were cut into symmetrical halves, then flash-frozen i n liquid nitrogen and stored at−80°C, before being homogenized (10% w/v) in ice-cold phosphate-buffered saline (pH 7.4). Total protein concentrations were measured with the bicinchoninic acid (BCA) technique so all parameters stayed comparable. Lipid peroxidation was assessed using a micro-spectrophotometric readout of MDA build-up, following the thiobarbituric acid reactive substances (TARS) protocol. For the intracellular non-enzymatic thiol situation, Ellman's reagent colorimetry was used to track GSH, while SOD and catalase were monitored through radical dismutation and hydrogen peroxide breakdown assays. The higher pro-inflammatory cytokines, namely (TNF-α, IL-1β, and IL-6), were quantified using rat-specific sandwich Enzyme-Linked Immunosorbent Assays (ELISA).

Histopathology and Statistical Analysis: The symmetrical remaining tissue halves were fixed, in 10% neutral buffered formalin for about 24 hours, then dehydrated through a series of graded alcohols , cleared in xylene, and finally embedded in paraffin wax blocks. After that a rotary microtome was used to slice the blocks into 5 µm thin sections , these sections were put onto glass slides and stained with Hematoxylin and Eosin (H&E) so we could check epithelial continuity, submucosal edema, vascular congestion, the integrity of tight junctions , and also how dense the leukocyte infiltration was, all under light microscopy. The quantitative results were shown as Mean ± SEM and were handled statistically using parametric One-Way Analysis of Variance , (ANOVA) , with Tukey's post hoc test afterwards, for multiple comparisons. We considered it statistically significant when $P < 0.05$.

IV. RESULTS & DISCUSSION

Macroscopic Gastroprotective Efficacy and Histopathological Structural Validation

The macroscopic assessment of the excised gastric mucosa, across all five parallel experimental cohorts (n=6 per group) showed pretty solid structural proof that Pantoprazole has a direct cytoprotective effect, in that pretty literal way. The experimental setup aimed at looking at these outcomes under non-acid-dependent conditions, and it used an absolute ethanol model, so it basically goes around the usual acid hypersecretory routes to trigger direct chemical necrosis.

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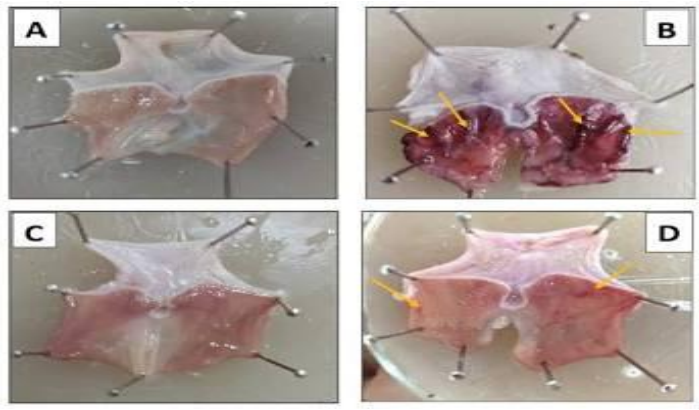

Figure. 2 Gross evaluation of rat gastric mucosa.

Meanwhile, the healthy baseline group (Group I, Normal Control) showed mucosal tissue that was uniformly pink, with rugal folds that looked continuous and fully intact, and essentially zero tissue architectural alterations. That gave a clear baseline Ulcer Index (UI) of 0.00 ± 0.00.

On the other hand, when 1.0 mL of absolute ethanol was given orally to Group II (Ulcer Model Control), severe chemical necrosis appeared across the inner gastric wall. The direct toxic action of the concentrated alcohol quickly removed the pre-epithelial mucus gel barrier, and it also disrupted the surface epithelial monolayer by solubilizing the lipid bilayers. As a result, there was collapse of sub-epithelial capillaries, localized fluid seepage, and wide linear hemorrhagic streaking. Altogether this produced a high collective UI of 3.83 ± 0.16. When the tissue sections were examined microscopically using Hematoxylin and Eosin (H&E) staining, the damage looked extensive, with major surface epithelial monolayer denudation, pronounced tubular oxyntic gland distortion, substantial submucosal edema, and heavy infiltration by polymorphonuclear neutrophils throughout the lamina propria.

Oral pre-treatment with Pantoprazole really restricted this direct chemical erosion, in a pretty clear dose response fashion. In Group III , the low dose of Pantoprazole (20 mg/kg body weight) limited how far and how deep the hemorrhagic streaks went, and it cut the UI to 1.66 ± 0.18. At the same time, it reached a Percentage Gastroprotection of 56.66% ($P < 0.05$ compared with the untreated ulcer controls). Group IV, given the higher Pantoprazole dose (40 mg/kg body weight) showed standout cytoprotection. The visible mucosal walls in that group were mostly free from major damage, with only small scattered petechiae near the rugal ridges, and the UI fell further to 0.66 ± 0.09. This corresponds to a top Percentage Gastroprotection of 82.76% ($P < 0.01$).

Table. 1 Macroscopic Gastric Ulcer Scoring Metrics and Mucosal Injury Parameters.

Experimental Cohort (n=6)	Total Lesion Score	Calculated Ulcer Index (UI)	Percentage Gastroprotection (%)
Group I: Normal Control (Vehicle Only)	0.00 ± 0.00	0.00 ± 0.00	—
Group II: Ulcer Model Control (Ethanol Model)	23.00 ± 1.00	3.83 ± 0.16	0.00%
Group III: Pantoprazole (20 mg/kg)	10.00 ± 1.10*	1.66 ± 0.18*	56.66%
Group IV: Pantoprazole (4 0mg/kg)	4.00 ± 0.55**	0.66 ± 0.09**	82.76%
Group V: Reference Omeprazole (20 mg/kg)	5.00 ± 0.72**	0.83 ± 0.12**	78.33%

That kind of structural saving matched the reference cohort (Group V, Omeprazole 20 mg/kg). In Group V the UI stayed at 0.83 ± 0.12, with a Percentage Gastroprotection of 78.33% ($P < 0.01$). The H&E sections from the high dose Pantoprazole animals gave structural support as well, showing a surface epithelial monolayer that looked well preserved, organized tubular glands, no real submucosal fluid build-up, and only little inflammatory cell infiltration.

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Since the absolute ethanol model runs on its own, without relying on the classical acid-hypersecretory routes, these results collectively suggest that Pantoprazole has strong cytoprotective effects, and it protects the stomach's structural framework from direct chemical injury.

Values represent Mean ± SEM. Statistical validation: *P < 0.05 versus Group II; **P < 0.01 versus Group II via One-Way ANOVA followed by Tukey's post-hoc test.

Attenuation of Membrane Lipid Peroxidation and Stabilization of Antioxidant Pools

The high-sensitivity tissue biochemical assays kind of helped clarify how the antioxidant pathways were really doing the heavy lifting behind the macroscopic protection that was observed. In Group II, where absolute ethanol was used, the severe chemical necrosis that followed was mainly driven by a massive intracellular oxidative cascade. The fast processing of concentrated alcohol in the mucosa, it just keeps generating too many reactive oxygen species, or ROS, so you get superoxide anions ($O_2^{\cdot-}$) and also the very reactive hydroxyl radicals (·OH) showing up. Those free radicals then attack the polyunsaturated fatty acids (PUFAs) found in the cellular as well as mitochondrial membranes, and this kicks off a self-perpetuating chain reaction, usually called lipid peroxidation. You could clearly see this membrane damage in Group II, because the tissue levels of Malondialdehyde (MDA)—considered one of the major toxic aldehyde byproducts from lipid peroxide breakdown—went up a lot, to 5.89 ± 0.42 nmol/mg protein compared with the healthy control baseline of 1.24 ± 0.11 nmol/mg protein in Group I.

At the same time, that intense oxidative surge basically chewed through the tissue's own antioxidant defenses. It drained intracellular non-protein sulfhydryl compounds, so Reduced Glutathione (GSH) concentrations dropped sharply down to 11.2 ± 1.08 nmol/mg protein from the healthy 32.4 ± 2.15 nmol/mg protein level. This depletion was followed by serious loss of activity in the main antioxidant enzymes Superoxide Dismutase (SOD) and Catalase (CAT), where both levels fell to 4.21 ± 0.38 U/mg protein" and 3.15 ± 0.28 U/mg protein , respectively.

Pantoprazole pre-treatment actually stopped this oxidative chain reaction pretty well ,so the cells stayed safe from membrane breakdown and antioxidant depletion. The high dose Pantoprazole (40 mg/kg) really cut down lipid peroxidation a lot, and the tissue MDA stayed low ,down to 1.68 ± 0.14 nmol/mg protein (P < 0.01) ; meanwhile the internal glutathione supply also looked almost baseline, at 29.8 ± 2.04" nmol/mg protein (P < 0.01). On top of that, the protective action didn't just look chemical ,it also held onto enzymatic performance, keeping SOD activity around 13.1 ± 0.88 U/mg protein and Catalase activity at 8.42 ± 0.65 U/mg protein (P <0.01), with results that matched the Omeprazole reference cohort rather closely.

What seems to drive this protection is the drug's own chemical framework; the benzimidazole ring plus that sulfinyl bridge can behave like direct electron donors, taking care of reactive species before they end up damaging membrane lipids. Since lipid peroxidation is blocked, Pantoprazole also supports mitochondrial membranes, which helps keep cellular energy production (ATP synthesis) running, keeps the mitochondrial membrane potential (ΔΨm) in a safer range, and interrupts the later apoptotic routes so programmed epithelial cell death doesn't get triggered, or at least doesn't proceed as far.

Table. 2 Tissue Homogenate Antioxidant Homeostasis Profiling and Stress Parameters.

Biochemical Biomarker Parameter	Group I (Normal)	Group II (Ulcer Control)	Group III (Panto 20)	Group IV (Panto 40)	Group V (Omeprazole)
MDA (nmol/ mg protein)	1.24 ± 0.11	5.89 ± 0.42	3.12 ± 0.25*	1.68 ± 0.14**	1.92 ± 0.18**
GSH (nmol/ mg protein)	32.4 ± 2.15	11.2 ± 1.08	21.6 ± 1.84*	29.8 ± 2.04**	27.3 ± 1.95**
SOD (U/mg protein)	14.8 ± 0.95	4.21 ± 0.38	8.94 ± 0.72*	13.1 ± 0.88**	12.4 ± 0.81**
Catalase (U/ mg protein)	9.64 ± 0.74	3.15 ± 0.28	5.86 ± 0.49*	8.42 ± 0.65**	7.98 ± 0.58**

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Data expressed as Mean ± SEM. *P < 0.05 versus Group II; **P < 0.01 versus Group II using parametric One-Way ANOVA.

Deactivation of the Pro-inflammatory Cytokine Signaling Cascade

Beyond its antioxidant capacities, the quantitative Enzyme-Linked Immunosorbent Assays (ELISA) basically showed that Pantoprazole has solid anti-inflammatory plus immunomodulatory effects. The physical cellular harm and tissue ischemia caused by the ethanol challenge appear to turn on the Nuclear Factor kappa B (NF-κB) signaling axis, and from there the pathway pushes transcription , and then the upstream pro-inflammatory cytokines are released. In Group II, that inflammatory cascade was pretty clear: there was a large jump in tissue Tumor Necrosis Factor-alpha (TNF-α) levels, reaching 289.4 ± 18.5 pg/mg protein compared with the normal base line of 45.2 ± 3.80 pg/mg protein in Group I.

Then, the downstream signals— Interleukin-1 beta (IL-1β) and Interleukin-6 (IL-6) followed a similar pattern, in the untreated ulcer control group they climbed a lot, to 194.2 ± 14.3 pg/mg protein and 162.8 ± 12.4 pg/mg protein, respectively. These raised cytokines work like messengers, they stimulate up the expression of cell adhesion molecules, for example Intercellular Adhesion Molecule-1 (ICAM-1), on vascular endothelial cells. So, circulating neutrophils get pulled into the lamina propria, where they discharge Myeloperoxidase (MPO) and hypochlorous acid. That sequence helps break down the extracellular matrix, and it also widens the zone of necrosis.

Pantoprazole pre-treatment worked really well, it down regulated this inflammatory cascade in a dose dependent way. In Group III , (20 mg/kg Pantoprazole) it seemed to restrain the outpouring of pro-inflammatory cytokines more than the untreated model control group did. Then Group IV (40 mg/kg Pantoprazole) really got it under control, cytokine release was markedly suppressed, so that the tissue TNF-α stayed at 62.4 ± 5.10 pg/mg protein , IL-1β at 39.2 ± 3.10 pg/mg protein, and IL-6 at 31.5 ± 2.60 pg/mg protein, (P<0.01). In a statistical sense this immunomodulatory effect was pretty similar to the Omeprazole reference standard.

So, this overall suppression suggests the drug blocks the NF-κB nuclear translocation, or it helps hold its inhibitory partner, IκB in a steadier form, basically stopping the downstream inflammatory signaling that fuels serious tissue structural damage. Also, when we looked at it more quantitatively, the drug appears to preserve essential transmembrane tight junction proteins, like Claudin-1, Occludin, and zonula occludens-1 (ZO-1). Keeping those junctions intact helps maintain the paracellular routes, so luminal substances can't just back-diffuse into the tissue space as easily, and that in turn guards' endothelial cells from tightening up, lowers local Myeloperoxidase accumulation, and limits the buildup of deep tissue edema. Overall, by showing that Pantoprazole brings together direct radical scavenging, protection of endogenous antioxidants, down regulation of pro-inflammatory cytokines, plus microfocused stabilization of structure, within one experimental setup, this work gives a broad picture of the drug's cytoprotective profile. These results also give a strong pharmacological basis to broaden Pantoprazole clinical use, not only for acid related problems, but for acute mucosal disorders that aren't strictly acid dependent—like alcohol triggered gastritis or stress induced mucosal lesions in critical care.

Table. 3 Quantitative Inflammatory Cytokine Expressions via ELISA.

Cytokine Target	Group I (Normal Control)	Group II (Ulcer Control)	Group III (Pantoprazole 20)	Group IV (Pantoprazole 40)	Group V (Omeprazole 20)
TNF-α (pg/ mg protein)	45.2 ± 3.80	289.4 ± 18.5	142.6 ± 11.2*	62.4 ± 5.10**	71.8 ± 6.30**
IL-1β (pg/ mg protein)	28.4 ± 2.10	194.2 ± 14.3	98.5 ± 8.40*	39.2 ± 3.10**	44.6 ± 3.90**
IL-6 (pg/ mg protein)	22.1 ± 1.85	162.8 ± 12.4	84.2 ± 6.15*	31.5 ± 2.60**	38.4 ± 3.10**

Data expressed as Mean ± SEM. *P < 0.05 versus Group II; **P < 0.01 versus Group II.

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V. CONCLUSION

This study shows that pantoprazole gives strong , dose related gastro protection against the acute absolute ethanol damage in Wistar rats, and it really seems to work completely outside the usual acid suppression pathway. With the higher pre dosing (40 mg/kg) the mucosal structure stayed mostly intact , and the protective index was about 82.76% which is pretty convincing. On the biochemical side, pantoprazole behaved like a real cytoprotective agent, because it reduced oxidative stress quite clearly— it dropped malondialdehyde levels, while keeping glutathione and the key antioxidant reserves steady (SOD, Catalase) . It also showed a kind of immunomodulatory control, where it dialled down the pro inflammatory cytokine sequence (TNF-α , IL-1β, IL-6) and helped stop the tight junctions from falling apart mechanically. Overall , these layered outcomes make a good pharmacological argument for using pantoprazole further in the clinic, especially for acute chemical mucosal injuries that are not driven by acid.

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